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TABLE OF CONTENTS FIRST PAGE

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VOLUME 68 SEPTEMBER 1952 NUMBER 3

BRAIN OF PATIENT A. AFTER BILATERAL FRONTAL LOBECTOMY; STATUS OF FRONTAL-LOBE PROBLEM

RICHARD M. BRICKNER, M.D.
NEW YORK

PATIENT Joe A., on whom Dr. Walter Dandy performed a bilateral frontal lobectomy in 1930, died Aug. 31, 1949. Clinical descriptions have previously been recorded.[1] The necropsy is reported in this paper.

A. was the first human being to undergo bilateral frontal lobectomy. Studies of A. were reported at the International Congress of Neurology in London in 1935. Egas Moniz was present at this meeting, where he described some of his early work on cerebal angiography. In the thinking which led him to initiate lobotomy, Moniz was much influenced by the London report of A.'s postoperative behavior and by Fulton and Jacobsen's description of chimpanzee behavior after a similar operation, described at the same meeting.[2]

Study of A. also has added to our understanding of frontal-lobe function. The role of *loss* of frontal tissue in symptom production has recently been minimized; some workers believe that the presence of pathological tissue is far more important. This matter will be discussed in the present communication.

REPORT OF NECROPSY

Necropsy, made about 50 hours after death, was limited to the head and was performed by Dr. Joseph Globus.

Summary of Significant Findings.—1. Gross examination of the skull showed bilateral frontoparietal deformities; the area on the left side of the head was soft,

This study was supported in part by the Fund for Research, Inc.

From the Neurological Service, the Mount Sinai Hospital; Dr. I. S. Wechsler, Chief Neurologist.

Read at the Seventy-Sixth Annual Meeting of the American Neurological Association, June 12, 1950, Atlantic City, N. J.

1. (*a*) Brickner, R. B.: Interpretation of Frontal Lobe Function Based upon Study of a Case of Partial Bilateral Frontal Lobectomy.: Localization of Function in the Cerebral Cortex, A. Res. Nerv. & Ment. Dis., Proc. (1932) **13**:259, 1934; (*b*) Intellectual Functions of the Frontal Lobes: A Study Based upon Observation of a Man After Partial Bilateral Frontal Lobectomy, New York, The Macmillan Company, 1936; (*c*) A. was originally referred to me by the late Dr. Joseph Brettauer. In recent years the patient had been under the care of Dr. Catherine Tyson.

2. (*a*) Egas Moniz: Tentatives opératoires dans le traitement de certaines psychoses, Paris, Masson & Cie, 1936; (*b*) How I Came to Perform Prefrontal Leucotomy, in Psychosurgery, First International Conference, Lisbon, Livraria luso-espanhola, 1949, pp. 15-21. (*c*) Freeman, W., and Watts, J. S.: Psychosurgery, Ed. 1, Springfield, Ill., Charles C Thomas, Publisher, 1942. (*d*) Abstracts of Second International Neurological Congress, London, 1935, p. 70. (*e*) Crawford, M. P.; Fulton, J. F.; Jacobsen, C. F., and Wolfe, J. B.: Frontal Lobe Ablation in Chimpanzee! A Résumé of "Becky" and "Lucy," A. Res. Nerv. & Ment. Dis., Proc. (1947) **27**:3, 1948.

and that on the right hard, to the touch. This was because the bone flap of the wound on the right side had apparently been replaced, whereas on the left side the

Fig. 1.—Ventral view of the brain. The rather sharp edge of the frontal stump shows plainly.

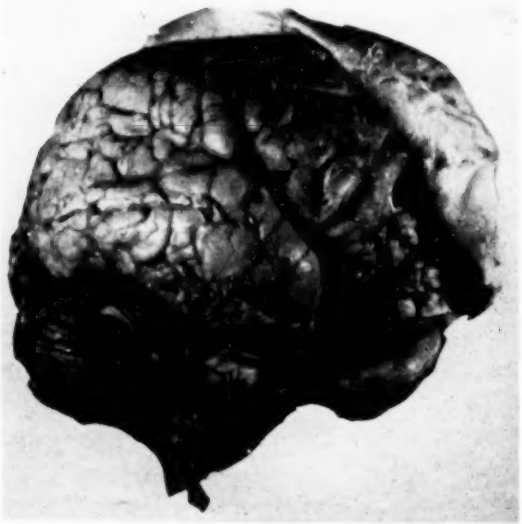

Fig. 2.—Right side of the brain prior to removal of the dura. The filmy adhesions binding the dura to the operative area are shown.

bone had not been replaced, and the scalp and underlying tissue (dura) were adherent.

2. Both frontal lobes had been removed (Figs. 1 to 4).

3. The frontal stumps were connected with the dura by filmy adhesions.

4. There was no evidence that the blood supply from either anterior cerebral artery or from any other major blood vessel had been impaired.

5. A meningioma was found, adherent to the stump of the left frontal lobe; its greatest diameter was about 2 cm. Several apparently implanted, very small meningiomas were scattered over the ventral surface of the tentorium. A large meningioma occupied most of the white matter of the right occipital lobe (Figs. 5 to 7).

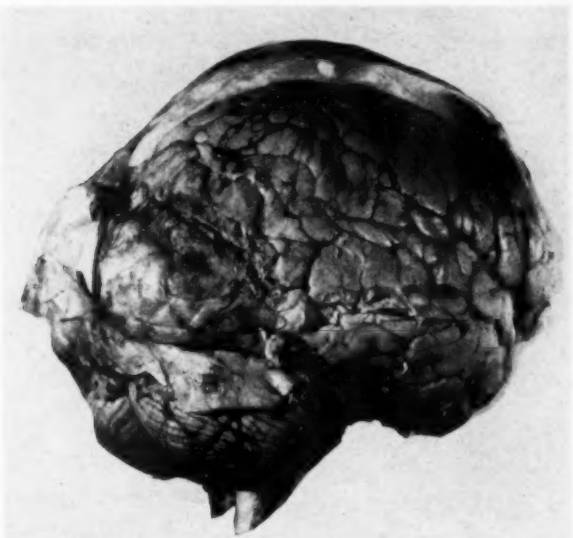

Fig. 3.—Right side of the brain, with most of the frontal lobe missing.

Additional Notes.—Removal of the scalp where it overlay the deformities was difficult. Particularly on the left side, the scalp was firmly attached to the underlying tissue, which was apparently dura.

The bony defect on the left measured about 12 cm. (anteroposterior diameter) by 4 cm. The deformity extended almost from the rostral end of the frontal bone back to the parietal bone and included some of the temporal bone. The bony deformity on the right was limited to the frontal bone and formed a rough circle about 5 cm. in diameter. The bone flap had apparently been reinserted at the time of operation, and the wound was well healed. The one metal suture present was broken through, and the overlying scalp was blackened. The external surface of the reinserted bone flap was gnarled; its inner surface was much flatter. The dura was firmly adherent to the edges of the bony defect on the left and to the bone flap on the right. The internal cranial surface was otherwise not unusual.

In removing the scalp and cranium, the dura under the defect on the left was inadvertently opened and the left ventricle apparently entered. For the most part the brain was removed with the dura attached.

Microscopic Study.—The subtentorial tumor tissue had a marked uniformity; the predominant cells resembled fibroblasts of fairly mature type, often arranged in large whorls. In many places they were sparsely packed for the cells of a meningioma. In some places they assumed a cuboidal shape, giving the appearance of fatty tissue. With higher magnification it was seen not only that these cells were enlarged and degenerating fibroblasts but that some of them were compound granular cells. The zones of these cells were reminiscent of the areas of degeneration in the embryonal meninges when the arachnoid splits from the pia. The vascular

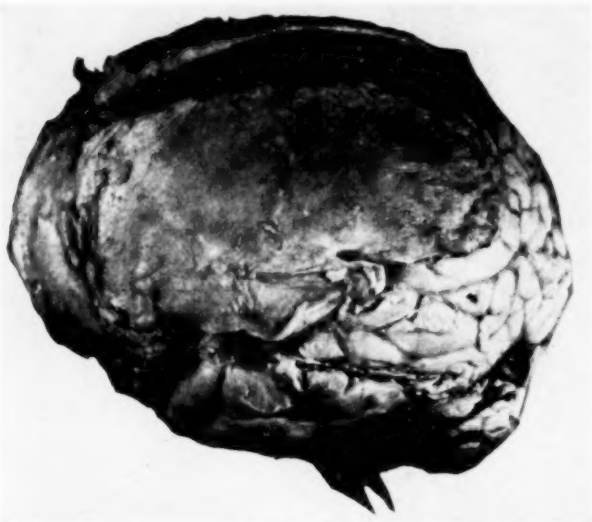

Fig. 4.—Left side of the brain, with most of the frontal lobe missing. The dura is adherent to the surface of the brain.

component of this tumor was of moderate proportion. The diagnosis was pial meningioma of fibroblastic type.

Sections of the frontal tumor showed essentially two types of tissue. The first consisted of streams of cells with large, oval nuclei and abundant cytoplasm, frequently forming whorls, with a blood vessel in the center. Vascularity was moderate in amount. One of the sections was crowded with foam cells. The second type consisted of streams of highly typical fibroblastic cells, also forming whorls. The diagnosis was pachyleptomeningioma.

Sections of the occipital tumor exhibited the same two types of tissue as those just described for the other tumors. In addition, there were many psammoma bodies. Contiguous cortex showed disrupted cytoarchitecture with many neurons undergoing degenerative changes. The diagnosis was pachyleptomeningioma.

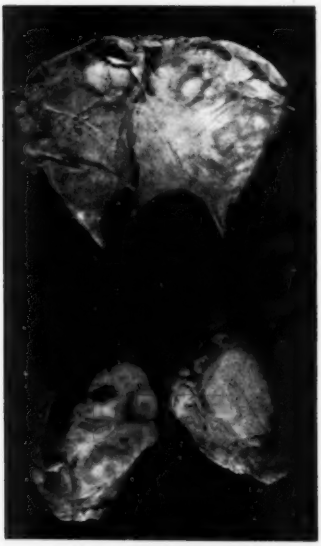

Fig. 5.—Upper part: Ventral surface of the tentorium with small meningiomas. Lower part: Section of the tip of the occipital lobes, the right containing a meningioma.

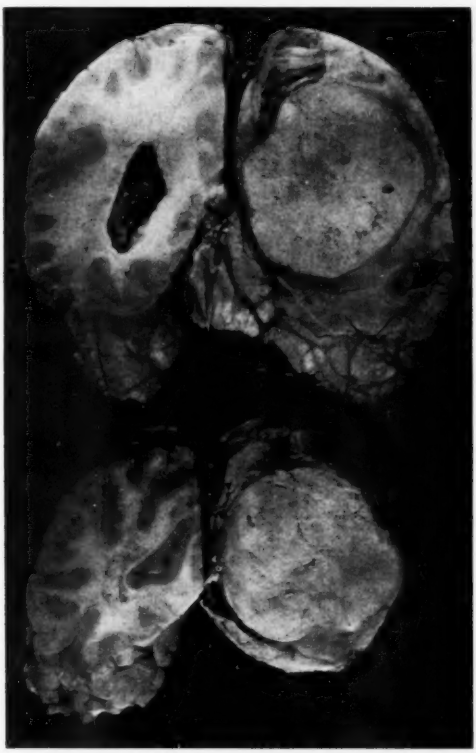

Fig. 6.—Sections of the occipital lobes, the right containing a meningioma.

The pituitary gland showed a high degree of basophilic hyalinization and contained many hyalinized and calcified blood vessels.

POSSIBLE RELATION OF TUMORS FOUND AT AUTOPSY TO A.'S SYMPTOMS

1. The tumor adherent to the left frontal stump could not have been present at the time of the operation, or it would have been seen.

2. That the occipital tumor was absent in 1931 is suggested by the evident normality of the visual fields, as tested by Dr. Isador Goldstein at that time.[3] In retrospect, the left temporal field seemed slightly more constricted than the right;

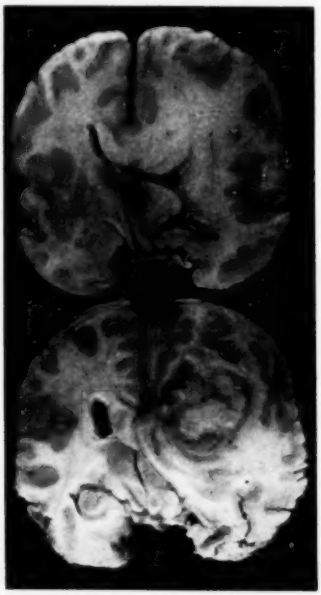

Fig. 7.—Sections through the anterior part of the occipital lobes, showing the anterior termination of the tumor. The upper section, which is the more anterior, shows no actual tumor tissue grossly.

this difference should not be ignored, even though it was so slight as to be considered without significance.

3. The likelihood that the newly found tumors were present when A. was first studied in 1931 is very slight, partly because there was no clinical indication of any expansion for many years. From 1930 until late in 1944 A.'s behavior remained virtually unchanged, the slight changes which did occur consisting of such details as an increased willingness to bathe.[4] In fact, A. lacked all the development and

3. Brickner, 1b p. 12.

4. Brickner, R. B.: Bilateral Frontal Lobectomy: Follow-up Report of a Case, Arch. Neurol. & Psychiat. **41**:580, 1939.

change which intact persons undergo over a long period of years.[4] Late in 1944 he began to have attacks of weeping, easily provoked by the mention of friends who had died before his operation. The weeping would end in a few seconds, and A. would resume his habitual jovial mood and behave as though nothing had interrupted it. At the same time, his rages became somewhat more intense, though no more frequent. These reactions may have represented clinical evidence of the presence or growth of the occipital tumor. If so, they were the first such evidences.

No further clinical evidence of either the existence or the growth of these tumors occurred until 1947, when real evidence appeared. In 1947 A. began to lose the alertness which had never before been impaired. Left hemiparesis appeared. The frontoparietal operative defect, which had always been soft, sunken, and pulsating, then became distended and lost its pulsation. Until then, no change in the physical status had been discovered.

Between 1947 and 1949 the evidence of pyramidal-tract involvement on the left increased; spasticity of the left extremities increased, and they became completely paralyzed. Left facial paresis also appeared. Frequent vomiting began; a large amount of weight was lost, and general weakness developed. Thes symptoms gradually advanced until, with signs of pneumonia, A. died. The fundi could never properly be examined. Dandy never performed pneumoencephalography on A., and A.'s family forbade it later. Periodic roentgenograms of the skull from 1931 to 1947 showed no change in the position of the silver clips put in during the operation.

Worth noting in passing is a fragment of A.'s behavior indicating how firmly fixed and how automatic units of behavior can become, even when acquired relatively late in life. A few weeks before his death, when A. was very weak, I entered his room, after a considerable absence. A., although on his back in bed, greeted me by making the punching postures which he had used for that greeting for many years; lacking strength to speak audibly, he whispered the words which had always accompanied the posturing, "And I can do it, too."

4. The first electroencephalogram, done by Dr. Hans Strauss on Nov. 4, 1940 (over 10 years after operation), showed "very slight decrease in voltage in the right occipital region, which is not definitely abnormal." In retrospect, this may have signified the presence of the occipital tumor.

No evidence of diffuse dysfunction was found in 1940. "Slight diffuse cerebral dysfunction" was reported for the first time in the next electroencephalogram, taken May 1, 1940. The same finding, but less conspicuous, was reported on March 15, 1947. Marked diffuse dysfunction and definite evidences of the occipital tumor were reported, both for the first time, on Nov. 1, 1947; hence there was evidence of rapid change in 7½ months. These last electroencephalographic changes coincided with the onset of dural bulging and changes in the clinical picture described above.

In all electroencephalograms delta activity appeared in the frontal leads bilaterally. This was assumed to be the consequence of the amputations. Possibly this abnormal electrical activity may have had a bearing on the behavioral disturbances. Yet Hebb and Penfield's patient still had postoperative evidence of electrical abnormality on one side when free of gross "frontal lobe" symptoms. These authors stated:[5]

Two electroencephalographic examinations were made. On one occasion no abnormality of electrical potentials was discovered. On the other the following report was made: "Bursts of

5. Hebb, D. O., and Penfield, W.: Human Behavior After Extensive Bilateral Removal from the Frontal Lobes, Arch. Neurol. & Psychiat. **44**:421, 1940.

3 per second waves were no longer present, and epileptiform spikes were no longer obtained in the right frontal region. On the left side no abnormal activity was obtained from the preoperative focus, but there was suggestive evidence of a mildly active focus of epileptiform activity in the posterolateral frontal region. Here, there occurred occasional random spikes."

Comment.—Presence of the tumors in 1931 without detectable growth until much later is, of course, highly unlikely. Even if they were present, these tumors could hardly have been the major cause of A.'s mental and emotional picture at that time, with his massive amputations playing a slight or no role. To suppose that they were the major cause would be to assume (*a*) that the loss of some occipital tissue was more important than the loss of both frontal lobes, a wholly gratuitous assumption, or (*b*) that tissue loss is unimportant and the presence of pathological tissue, even if small in amount and far from the frontal lobes, is all-important in explaining "frontal lobe symptoms" as we understand them.

It is possible that residual pathological tissue, while not basically responsible for the symptom picture in a case of lobectomy, may intensify or color it.

What appears to be incontrovertible evidence that A.'s symptoms resulted from his amputations, and not from any possible residual tumor tissue, is the fact that the symptoms developed coincidentally with his recovery from the surgical procedure, there having been no such phenomena prior to the operation. Before operation A. was mentally well, so far as any one, including a competent neurologist whom A. consulted for headache, could tell; he was doing his work and functioning normally in his social relations until he suddenly went into coma. The operation was performed during this coma. When the "frontal lobe symptoms" developed after operation, there was, of course, far less pathological tissue present than in A.'s preoperative, symptom-free period. Dandy believed, in fact, that removal of the tumor was complete.

In summary, there is no evidence for the existence of the newly found tumors at the time A. was studied. The first detectable, questionable clinical evidences of their presence appeared late in 1944; the first real evidences occurred in 1947. The first electroencephalogram (1940) gave questionable evidence of a right occipital lesion; the first substantial evidence was found on Nov. 1, 1947. All the solid evidences for the presence of the occipital tumor, and for its enlargement, began in 1947.

EFFECTS OF FRONTAL-TISSUE LOSS

Some believe that the tissue losses in lobectomy and lobotomy are of slight or no consequence in explaining those ensuing phenomena which are known, although every author believes the tissue loss must have some effect. In some instances the sequelae oftenest attributed to loss of tissue are said to be absent. Hence, the authors believe, the "usual" sequelae are probably due to something else, such as the influence of pathological tissue, and whatever sequelae do result from the loss of tissue are still unknown. Earlier, investigators occasionally voiced a similar idea [1b]; they invoked "toxins" from pathological tissue in the brain to explain the phenomena. Workers of today think in terms of abnormal electrical effects produced by pathological tissue.

Obviously, the tumor itself may influence the preoperative symptom picture, for some patients improve symptomatically after extirpation of the tumor without radical tissue removal, in circumstances in which increased intracranial pressure seems not to play a role. Tissue distant from the tumor may be affected through

distortion of the brain or interference with blood supply; aside from the factor of increased intracranial pressure, hemisphere tumors near the midline may, in addition, compromise the opposite side by direct pressure.

Quite possibly, many of these distant effects may persist even after complete removal of the tumor. Any which do persist would necessarily be the result of tissue loss, cells having died from the action of the factors just named. However, the fact that a lesion as such may affect brain function certainly does not preclude the probability that amputation also affects function.

A bringing together of the evidence relevant to this question may help to clarify it. The case of A. is perhaps especially appropriate as a basis for such a discussion, since his tissue losses were massive but autopsy, albeit almost 20 years later, disclosed pathological tissue in addition.

CASES OF HUMAN FRONTAL LOBECTOMY AND METHODS OF STUDY

The present period of study of frontal lobe function began with the advances in neurosurgery which made human lobectomy possible. Dandy was the surgical instigator of all the interesting developments which have followed. He recorded his first unilateral frontal lobectomies in 1922, reporting no observable mental or other sequelae.[6] In 1928 his first hemispherectomies, five in number, were described as equally barren of behavioral disturbances.[7]

Unilateral lobectomies by other surgeons followed in some numbers, and hemispherectomies and bilateral lobectomies have also been recorded. The four patients with hemispherectomy reported by Karnosh and Gardner showed no definite behavioral or mental changes.[8] O'Brien, reporting a case in which Gardner had operated, came to a similar conclusion [9]; Zollinger's [10] patient with hemispherectomy (dominant side) was aphasic and hence could not be studied behaviorally.

None of these patients was studied in psychological detail; and in view of later, very thorough, studies of lobectomy patients, there is room for some doubt concerning the reported absence of change. Obviously, if there were any changes, they did not appear grossly.

The first detailed observations on patients after frontal lobectomy were presented at a meeting of the Association for Research in Nervous and Mental Disease in 1932. Two cases of unilateral frontal lobectomy were reported by German and Fox; two, by Penfield and Evans, and the case of A., by me. German and Fox [11] reported that in one case, after removal of a major portion of the nondominant frontal lobe, there was "no observable intellectual defect," whereas in their second case, after removal of a smaller portion of the dominant frontal lobe, there resulted

6. Dandy, W.: Treatment of Nonencapsulated Brain Tumors by Extensive Resection of Contiguous Brain Tissue, Bull. Johns Hopkins Hosp. **33**:188, 1922.

7. Dandy, W.: Removal of Right Cerebral Hemisphere for Certain Tumors with Hemiplegia: Preliminary Report, J. A. M. A. **90**:823, 1928.

8. Karnosh, L. J., and Gardner, W. J.: Physical and Mental Capacity After Removal of Right Cerebral Hemisphere, Dis. Nerv. System **1**:343, 1940.

9. O'Brien, J. D.: Removal of Right Cerebral Hemisphere: Case Report, Ohio M. J. **28**:645, 1932.

10. Zollinger, R.: Removal of Left Cerebral Hemisphere: Report of a Case, Arch. Neurol. & Psychiat. **34**:1055, 1935.

11. German, W. J., and Fox, J. C., Jr.: Observations Following Unilateral Lobectomies: Localization of Function in the Cerebral Cortex, A. Res. Nerv. & Ment. Dis. Proc. **13**:378, 1932.

"definite impairment of intelligence, characterized chiefly by a paucity of spontaneous motor response." Moderate changes were noted by Penfield and Evans,[12] and severe ones, by me.[13]

At about the same time, Fulton and Jacobsen,[2e] and Jacobsen, Elder, and Haslerud[14] did thorough work with chimpanzees. They found impairment of memory and of delayed response reactions to be specific changes which followed bilateral, but not unilateral, lobectomy. The animal work will not be reviewed in this communication.

Ackerly described a patient who had been operated on by Spurling.[15] The right frontal lobe had been removed for extirpation of an oligodendroglioma, and the left frontal lobe was found to be reduced to a tab, so that bilaterality of involvement was pronounced. The changes in the patient's mentality and behavior were extensive. This study is notable not only because of the care and thoroughness with which it was made, but also because Ackerly gave great weight to actual observation of the patient, at the same time not neglecting psychometric tests. The changes in behavior shown by this patient were just as definite as those exhibited by A., but not so severe. Some of them, evidently, could have been overlooked had Ackerly been less assiduous. This author said that if any observation of fundamental significance could be obtained from his studies, it was the patient's apparent "difficulty in registering more than one stimulus at a time."

Karnosh's case of bilateral frontal lobectomy, reported next, was of high interest in showing long-standing disturbances closely resembling the manic-depressive cycle.[16] Karnosh thought that these disturbances in mood might be "the most common denominator among the sequelae" and might account for many of the other symptoms. In two other cases with nonsurgical damage to both frontal lobes there was similar evidence. Deficiency in the synthesis of complex ideas and absence of insight and of concern about health were also noted by Karnosh.

In the first few postoperative months Ackerly's patient had also shown symptoms suggestive of a hypomanic state, which he thought might underlie much of her

12. (*a*) Penfield, W., and Evans, J.: Functional Defects Produced by Cerebral Lobectomies, A. Res. Nerv. & Ment. Dis., Proc. **13**:352, 1932; (*b*) The Frontal Lobe in Man: A Clinical Study of Maximum Removals, Brain **58**:115, 1935.

13. Brickner.[1b] I was especially interested in changes in intellectual function and in the symptoms which I thought could be explained as consequences of such changes. I believed that an understanding of the effect of loss of frontal tissue upon intellectual processes would advance our knowledge of thought as a function of brain tissue. I concluded that the frontal lobes made possible a larger number of combinations of intellectual engrams than could otherwise occur. Their contribution to intellectual function was, in other words, quantitative; they added to it. Patient A. showed a deficit in the synthesis of complex combinations. It may be said at this point that most other workers who have found intellectual changes have reached conclusions which I believe to be similar in principle, although not in terminology. Rylander's conclusions concerning intellectual function seem, however, identical with mine, both in concept and in terminology.

14. Jacobsen, C. F.; Elder, J., and Haslerud, G.: Studies of Cerebral Function in Primates: I. Functions of the Frontal Association Areas in Monkeys, Comparative Psychology Monographs, Vol. 13, No. 3, Baltimore, Johns Hopkins Press, 1936.

15. Ackerly, S.: Instinctive, Emotional and Mental changes Following Pre-Frontal Lobe Extirpation, Am. J. Psychiat. **92**:717, 1935.

16. Karnosh, L. J.: Clinical Aspects of Frontal Lobe Disease, J. Indiana M. A. **28**:568, 1935.

symptom picture at that time. He was doubtful whether this condition was the result of tissue deprivation, but believed that it might have been "precipitated by the operation, accentuated by previous suffering, and [that it was] appropriate to her normal personality make-up." Of note is the reaction of the neighbors to Ackerly's patient. Their reliability was poor when it came to diagnosing a hypomanic state; they did not think "she has shown any unusual behavior, as she was always a very active person, almost to the point of restlessness. Five years before she was gay, facetious, lively and quick-tempered."

Karnosh's lobectomy patient continued in her mood changes indefinitely, however, varying from elation to depression. A., too, was in what appeared to be a permanent hypomanic mood. The fact that all three patients were hypomanic after operation, at least at times, suggests that the mood change may be a specific effect of the bilateral procedure. It is also possible that the facetiousness, euphoria, and witzelsucht which appear so often after frontal lobe impairment may make the general picture indistinguishable from a hypomanic state. In this connection Holmes's description of depression after frontal lobe lesions must also be taken into account.[17]

Jefferson's lobectomy cases were the next to be reported. He recorded a series of three cases of right and three of left lobectomy, which he described as showing that removal of the lobe on the dominant side was the same in its consequences as removal of the other lobe; thus, he attempted to answer a question which has troubled many students of the subject. No behavioral disturbances or "frontal lobe symptoms" were noted after postoperative recovery, but the behavioral and psychological observations were not sufficiently complete, as Jefferson himself stated.[18]

In two cases of Hyland and Botterell, both of unilateral lobectomy, there was no significant change, the report again being without intensive study.[19] The authors discussed thoroughly the theoretical differences between the effects of uni- and those of bi-lateral frontal lobectomy.[20]

The most extensive series in the literature was published by Rylander [21] in 1939. He reported 32 cases of unilateral lobectomy, and the quality and intensiveness of his work set a standard which will be hard to surpass. He traveled from place to place in Sweden, visiting the patients in their homes. In an effort to provide controls of the psychological tests he performed during these visits, he tested a relative or friend of each patient of approximately the same cultural and educational level

17. Holmes, G.: Mental Systems Associated with Cerebral Tumors, Proc. Roy. Soc. Med. (Sect. Neurol. & Psychiat.) **24**:65, 1931; abstracted, Brit. M. J. **1**:310, 1931; abstracted Lancet **1**:408, 1931.

18. Jefferson, G.: Removal of Right or Left Frontal Lobes in Man, Brit. M. J. **2**:199, 1937.

19. Intensive study includes thorough, prolonged observation of the patient's behavior, both in detail and *in toto*, and as thorough a comparison as possible of his preillness and postoperative states by careful, detailed questioning of persons who knew him well. A wide variety of tests should also be used. The tests must be of a nature to measure as many facets of personality as possible, and not merely of a type to measure intelligence quotients. It is of special importance to avoid depending entirely upon tests, without intensive personal observation of the patient.

20. Hyland, H. H., and Botterell, E. H.: Frontal Lobe Tumours: Clinical and Physiological Study, Canad. M. A. J. **37**:530, 1937.

21. Rylander, G.: (*a*) Personality Changes After Operations on Frontal Lobes: Clinical Study of 32 Cases, Acta psychiat. et neurol., Supp. 20, 1939; (*b*) London, Oxford University Press, 1939.

as the patient himself. He held thorough interviews with patient, friends, and family. His discussion of the balance between psychometric tests and direct observation of the behavior of the patient in evaluation of the consequences of lobectomy is thoughtful and comprehensive [22] and should be carefully heeded by anyone who proposes to study the problem. Rylander also made a considerable point of the relative ease with which changes may escape notice.

Most of Rylander's patients showed behavior changes, including intellectual deficits, subsequent to the operation; two did not. Rylander's work finally settled in the affirmative the question raised in Jefferson's investigation, namely, that losses of the right and left lobes are equipotential in their effects.

At about the same time Lidz's [23] study of a case of unilateral lobectomy was reported. Despite careful, thorough work, no behavioral sequelae were discovered.

The last of the contributions on the unilateral procedure was the series of Stookey, Scarff, and Teitelbaum.[24] These authors reported no postoperative behavioral changes when the whole tumor had been removed (six cases) and noted phenomena similar to those described by others when removal was incomplete (five cases). The studies were in no way comparable to Rylander's for thoroughness, so that, as with the reports of Jefferson and of Hyland and Botterell, the negativity of findings in six cases cannot be accepted with finality. If they could be, they would support the ideas of Hebb and of the Columbia-Greystone Project, discussed below. Undoubtedly, if there were any changes in the six cases which more thorough investigation might have detected, they were less gross and obvious than those in the other five, and certainly not as notable as the alterations following bilateral lobectomy presented by patient A. and the patients reported by Ackerly, Karnosh, and Nichols and Hunt (see below).[25]

Quite aside from his purely intellectual deficits, the changes in A.'s behavior were, however, as great as, or greater than, those of any other patient, regardless of the unilaterality or the bilaterality of the lobectomy. Karnosh's lobectomy patient may have shown lasting disturbances as prominent, and so may some of Rylander's patients. The condition of most patients was exceedingly abnormal for several weeks after operation. Quite possibly the hypomanic aspect and the euphoria and distractibility were what made A.'s changes so conspicuous, as was the case with Karnosh's patient. Yet one of the salient traits of A.'s case was his ability to pass as an ordinary person under casual circumstances, as when he toured the Neurological Institute in a party of five, two of whom were distinguished neurologists, and none of them noticed anything unusual until their attention was especially called to A. after the passage of more than an hour. In particular, A.'s impairment of intellectual performance as such was never conspicuous on casual examination.

Nichols and Hunt [25] reported another case of bilateral frontal lobectomy in which behavior was "far from normal." A great deal of dependence was placed on psychometric tests, but the patient's defects in spontaneous behavior were in agreement with what the tests showed.

22. Rylander,[21a] pp. 46-51.

23. Lidz, T.: Study of the Effect of Right Frontal Lobectomy on Intelligence and Temperament, J. Neurol. & Psychiat. **2**:211, 1939.

24. Stookey, B. P.; Scarff, J. E., and Teitelbaum, M. H.: Frontal Lobectomy in the Treatment of Brain Tumors, Ann. Surg. **113**:161, 1941.

25. Nichols, I. S., and Hunt, J. M.: A Case of Partial Bilateral Frontal Lobectomy: A Psychopathological Study, Am. J. Psychiat. **96**:1063, 1940.

The case of Mixter, Tillotson, and Wies [26] was not reported in such a way that one can be sure of what changes may have been due to the operation.

In only three of all the lobectomy cases in the literature, including both the unilateral and the bilateral cases, did careful study fail to show at least some of the symptoms we have regarded as results of frontal lobe deficit. These three are two of Rylander's cases and Lidz's case (all of unilateral lobectomy).

Frontal lobotomy frequently has behavioral consequences similar to those of lobectomy (unilateral and bilateral). As a rule, they are slighter in degree, except in the first few postoperative weeks, when they may be just as great as, or greater than, those of lobectomy. The similarity is of importance and should not be ignored.

CONCEPT THAT TISSUE LOSS IS WITHOUT KNOWN RESULTS

The conclusions of Hebb, in his follow-up report of Hebb and Penfield's case of bilateral lobectomy, are diametrically opposed to the general trend. If Hebb's ideas are correct, our whole view of frontal lobe function has to be changed. Their importance is thus great enough to require discussion in detail.

In 1939 Hebb [27] reported two new cases of unilateral lobectomy and one of extensive unilateral removal of frontal tissue. He also reexamined W. B., the patient previously reported on by Penfield and Evans [12a] at the 1932 meeting of the Association for Research in Nervous and Mental Diseases. The newly reported operations had been performed by Dr. W. Penfield and Dr. W. V. Cone: One was for abscess; one, for the removal of scar, and one (M. L.), for "an intracerebral cyst and calcification of surrounding tissue" (the case was later reported again by Harrower-Erickson [28] as one of cystic astrocytoma).

W. B., the old patient, did show some defects. Hebb stated that W. B. had been unemployed for several years and suggested that this situation, together with prolonged hospitalization, might explain his low intellectual status.[27] However, Penfield and Evans stated that this patient was employed in one position for seven of the eight years between the sustaining of his injury and the operation [12b] and that the longest period of hospitalization was two months.

The three new cases were reported as showing no postoperative changes, but Hebb relied exclusively on psychometric tests; no actual observations on the patients other than those connected with performance of the tests were reported. A year after operation, according to Harrower-Erickson's [28] later report, M. L. presented a behavior problem with pronounced antisocial tendencies; Hebb's studies had been made four months after the operation. M. L. could still work, however.

Case of K. M., with Bilateral Frontal Lobectomy.—Later, Hebb and Penfield [5] described a case of bilateral frontal lobectomy after which no definite, dependable changes in intellectual function or in general behavior were detected. In a thoughtful paper, the authors questioned whether the changes reported by others might not

26. Mixter, W. J.; Tillotson, K. J., and Wies, D.: Reports of Partial Frontal Lobectomy and Frontal Lobotomy Performed on Three Patients: One Chronic Epileptic and Two Cases of Chronic Agitated Depression, Psychosom. Med. **3**:26, 1941.

27. Hebb, D. O.: Intelligence in Man After Large Removals of Cerebral Tissue: Report of Four Left Frontal Lobe Cases, J. Gen. Psychol. **21**:73, 1939.

28. Harrower-Erickson, M. R.: Personality Changes Accompanying Cerebral Lesions: I. Rorschach Studies of Patients with Cerebral Tumors, Arch. Neurol. & Psychiat. **43**:859, 1940.

depend on factors other than the mere removal of tissue. Vascular change and necrosis in the rest of the brain as an operative complication, postoperative scarring, and the presence of additional, unknown lesions exercising pathological activity were invoked as possible explanations of the postlobectomy (or lobotomy) changes in previous cases.

K. M., had had a severe head injury at the age of 16. Fairly frequent seizures followed, which included an automatic state, in which he might strike any object in his path. Between attacks he was "irresponsible, childishly stubborn, restless and forgetful."

At operation a large cicatrix was found in both frontal lobes. It was densely attached to the dura. The alteration and destruction of the frontal lobes extended back to and included the tip of the anterior ventricular horn on both sides. The scar and a large part of each frontal lobe were extirpated.

The patient improved tremendously after the operation. Except for the immediate postoperative period, the patient failed to show the traditional gross signs of a frontal lobe lesion.

Less than five months after operation the authors reported no distractibility or impairment of restraint, or any other abnormality in intellectual function or general behavior, even though the circumstances of examination were somewhat trying to the patient. Recent memory was good, as far as could be ascertained. A year later the patient was seen again. Memory appeared excellent; other observations were not recorded.

Psychometric Tests: K. M.'s highest postoperative intelligence quotients were 98 (Stanford-Binet) and 75 (McGill revision of the Army Beta test).[29] (A., whose intelligence quotient varied, largely in terms of the attention he gave the tests, once achieved 99; the quotient of Nichols and Hunt's patient varied from 118 to 122.)

K. M. received a number of other psychological tests after operation which had not been administered prior to operation, and obtained good scores, in some instances better than the norm. Other observers had given a few of the same tests to other lobectomy patients, so that comparisons are possible. Comparative intelligence quotients have already been mentioned. K. M. could repeat six digits backward; A. was credited with repeating seven backward,[30] and his largest number repeated forward was eight. K. M. achieved a score of 7.5 with the Knox cubes; Nichols and Hunt's patient and A. each scored 6. Hence these tests do not reveal deficits which are evident in casual examination.

It is now known that many, if not all, of the conventional psychometric tests fail to reveal the deficits shown in other ways by patients after operation. Zubin [31]

29. An apparent improvement occurred in the results of the Stanford-Binet test; before operation, in a single test the intelligence quotient was 83; after operation four tests gave results of 94, 98, 98, and 94. (This apparent rise in the intelligence quotient is not conclusive, because the results in the different pairs of tests are not beyond the limits of error of the tests, nor are the differences great enough to exclude practice effects.) The McGill revision of the Army Beta test gave a preoperative score of 63; the postoperative scores were 71, 65, and 75. The single preoperative tests do not allow for the kind of variation appearing in the multiple postoperative tests.

30. Brickner,[1b] p. 257.

31. Zubin, J.: Rorschach Test, in Mettler, F. A., Editor: Selective Partial Ablation of the Frontal Cortex: A Correlative Study of Its Effects on Human Psychotic Subjects by the Columbia-Greystone Associates, New York, Paul B. Hoeber, Inc., 1949, Vol. 1, p. 295.

summarized the present status of this question in noting a general agreement that standard intelligence tests do not reveal any significant alteration after operation. The important question raised by Hebb,[27] "whether the ability of these three young men . . . to adjust themselves economically and socially is on the same plane as their intelligence test scores," has certainly been answered in the negative by Harrower-Erickson's study, at least for M. L.[28] M. L.'s intelligence quotient was 124, though a year later he was a behavior problem. However, K. M.'s results in the Rorschach test, reported separately by Harrower-Erickson,[32] resemble those of Harrower-Erickson's normal hospital-employee controls.[28] They lacked the stigmata of brain damage reported by Tallman and Klopfer[33] and by Piotrowski[34]; in fact, brain damage could not have been diagnosed from these findings. The results were wholly different from A.'s (the only other lobectomy patient to receive this test). Yet there was even greater disagreement between the clinical and the Rorschach findings in Case 8 of the Columbia-Greystone Associates[35]; a number of phenomena which regressed clinically were reported to show improvement in the Rorschach results.

Hebb and Penfield believed that later study of the patient might supply important information, stating[5]:

> It may be that only in such features as learning in social situations, in adaptation to drastic environmental change or in initiative and the ability to plan and organize one's affairs may be found the impairment that we believe must exist after large lesions of the frontal lobes, but of which we have found no evidence in the present case. It is clear that an apparent lack of effect on one type of ability does not mean that others are unaffected, as Lashley has pointed out, and further study of the rehabilitation of the patient may give some clue to behavioral defect following bilateral injury to the frontal lobes.

Follow-Up Report on K. M.: Six years after operation Hebb wrote further on K. M.[36] Tests with Goldstein's figures revealed no defect. The old tests were not repeated. Goldstein[37] later commented:

> In the light of our critique of I. Q. testing methods it seems not too far-fetched to suspect that the psychologic examination was not suited to reveal a defect. From what we have learned about the evaluation of my test results by Hebb such a possibility cannot be excluded.

Few direct observations on K. M. are mentioned. The family is quoted as calling the patient "normal in every way." A taxi driver, a waitress, and a storekeeper are quoted as saying, "There is nothing wrong with K. M.'s behavior now and . . . he is one of the most popular persons in the village." Such evidence is not very dependable; Ackerly's first patient was called normal by her neighbors when she

32. Harrower-Erickson, M. R.: Personality Changes Accompanying Cerebral Lesions: II. Rorschach Studies of Patients with Focal Epilepsy, Arch. Neurol. & Psychiat. **43**:1081, 1940.

33. Tallman, G., and Klopfer, B.: Rorschach Study of a Bilateral Lobectomy Case, Rorschach Res. Exchange, **1**:77, 1937. Klopfer, B., and Tallman, G.: A Further Rorschach Study of Mr. A., ibid. **3**:31, 1938.

34. Piotrowski, Z.: Rorschach Studies of Cases with Lesions of the Frontal Lobes, Brit. J. M. Psychol. **17**:105, 1937; Rorschach Inkblot Method in Organic Disturbances of the Central Nervous System, J. Nerv. & Ment. Dis. **86**:525, 1937.

35. Mettler, F. A., Editor: Selective Partial Ablation of the Frontal Cortex, Columbia-Greystone Associates, New York, Paul B. Hoeber, Inc., 1949, pp. 415-417.

36. Hebb, D. O.: Man's Frontal Lobes: Critical Review, Arch. Neurol. & Psychiat. **54**:10, 1945.

37. Goldstein, K.: Frontal Lobotomy and Impairment of Abstract Attitude, J. Nerv. & Ment. Dis. **110**:93, 1949.

was in a hypomanic state. A. seemed normal when seen casually by two neurologists; he was called different from his former self by friends who read his productions, but this was said ratther reluctantly and not with the striking clarity that might have been expected.

Of importance is the report that K. M. was in the Army and had been sent overseas. He was in uniform 10 months "before an epileptic attack, precipitated by hard labor, brought him to the medical officer's attention, when he was discharged."

What kind of work he did in the Army (a question raised by Goldstein [37]) and how he did it, how he related himself to his fellows and to the officers and what they thought of him, whether he was ever in trouble, and other points of importance, we do not know.

Hebb reported that K. M. has worked, finding jobs for himself (Hebb stated that this was during a wartime shortage of labor). Ackerly and Benton's patient (actually Ackerly's second patient), with no surgical removal of tissue but with massive bilateral frontal lobe destruction and many typical symptoms, also found it relatively easy to get jobs.[38] His first patient could do her housework. Thus, the ability to find jobs and do work is not evidence of freedom from "frontal lobe symptoms."

K. M. changed jobs frequently, having had "half a dozen since his discharge from the Army" (time interval not given). Ackerly and Benton's patient also never held a job for more than a few months because his performance was erratic. How disturbing or erratic K. M. may have been in his work is not reported.

The statement that an unexpected degree of initiative was suggested by K. M.'s "half-formed intention of going to Toronto" is not necessarily valid. A., for example, often declared his intention of resuming his old work on the stock exchange, but this was nothing more than boastfulness and the assertion of self-importance, because he had no idea of actually doing it. When an opportunity was given him to buy and sell some stocks, he put it off indefinitely with excuses, and never actually did anything about it.

Hebb [36] stated that K. M. was a "strikingly easy-going, carefree fellow, and his lack of concern for the distant future could be due to the cerebral excision." Hebb agreed that K. M.'s brother was not pleased with the frequent changes in jobs and that "in conversation K. M. showed no great concern about finding a job with permanence or future." He added that to prove that this was due to the lobectomy is another matter and that many normal persons have no more care for the morrow. Indifference to the future is, however, a frequent sequel to frontal lobe injury.

Many of the statements in Hebb's report are not documented, and the reader is left in doubt as to whether he is reading attested fact or supposition. For example, Hebb stated: "He is liked by his employers, as far as can be ascertained, and apparently other employers entice him away with offers of better working conditions, and so on." K. M. was in the process of quitting a job "for what was undoubtedly better working conditions" when Hebb saw him.

Hebb [36] added that A. and the patients of Nichols and Hunt and of Mixter, Tillotson, and Wies all needed continued care and detention. However, the patients of Ackerly and of Ackerly and Benton, full of symptoms as they were, were not in such need most of the time.

38. Ackerly, S., and Benton, A. L.: Report of Case of Bilateral Frontal Lobe Defect: Frontal Lobes, A. Res. Nerv. & Ment. Dis., Proc. (1947) **27**:479, 1948.

In the foregoing paragraphs is cited in full the evidence offered by Hebb in 1945 regarding K. M.'s actual behavior.

From the standpoint of detection of strictly intellectual defects, there is one factor which might have a considerable bearing on the evaluation of K. M.'s intellectual status. Rylander showed that intellectually untrained people "are not troubled by any noteworthy intellectual disturbances." Likewise (my interpretation) intellectually untrained friends and relatives of patients, such as those Hebb cited, may not observe changes in complex intellectual function. The patients Rylander referred to were laborers and farm hands. K. M. was also of this status.

This role of the patient's intellectual status in evaluation of the effects of brain injury was fully recognized by Hebb later (1949).[39] In discussing (page 280) the studies from which Halstead concluded that the generally accepted phenomena are the result of loss of frontal lobe tissue, Hebb criticized Halstead on the basis of insufficient data concerning occupation and sophistication and age factors, saying that Halstead's controls "do not meet the elementary requirements" in these respects. Hebb also stated that one must "use *clinical* controls, if one wishes to know not only that a certain kind of injury produces intellectual defects but also whether it produces more defect than some other kind of injury." Yet Hebb did not take K. M.'s intellectual status into account, nor did he use any controls at all in concluding that K. M. showed no recognizable defects.

Hebb also referred to the status of the patient of Mixter, Tillotson, and Wies as "indistinguishable from the normal" after his loss of frontal tissue (page 282),[39] although the data given by these authors are very meager. In his 1945 paper,[36] Hebb himself mentioned that this patient later had to be hospitalized in order that he be properly cared for.

It is entirely true that, superficially at least, K. M. differed from A. The latter could never have worked, and he could not have lasted a day in the army. However, there is nothing to show that the difference was more than one of degree (A's chronic hypomanic state must also be kept in mind in picturing the degree and conspicuousness of change), and nothing is presented to give a clear idea of what the two patients may have had in common. Many of the other patients described in the literature, careful study of whom showed the existence of changes, also differed from each other, and certainly from A., in the degree of change and in other respects.

It is certainly not evident to what degree K. M. differed from the other patients with either lobotomy or lobectomy. In some of them abnormalities were not readily apparent and had to be looked for. The joy of a patient's family at a patient's recovery from operation and improvement may obscure many of the more basic observations students of frontal lobe function are interested in, as Hebb and Penfield have suggested. This may have happened in the case of Mixter, Tillotson, and Wies; the parents described the patient as happily as K. M.'s family, but soon he had to live in a hospital. Something of the same nature may also have occurred in Ackerly's first case.

In his discussion, Hebb stated that "the small and diffuse region of partial necrosis can have a greater effect in the production of symptoms than a larger area of

39. Hebb, D. O.: Organization of Behavior, New York, John Wiley and Sons, 1949, pp. 279-282.

40. Footnote deleted.

complete destruction and cleancut removal of tissue." But no evidence is given for this.

This was done in accordance with the suggestion of Hebb and Penfield [5] that "the case in which the mental symptoms are fewest is likely to be best suited to the study of localization of function."

Hebb [41] discarded Rylander's conclusions. He also considered that in the case of A. the patient's postoperative "deterioration" fluctuated rather greatly and that therefore the cause could not have been a static loss of tissue. This idea rests on an oversimplification of brain function and fails to allow for the innumerable interwoven activities of the brain, which show themselves in normal, everyday life in such ways as shifts of mood and variations in capacity to think and function maximally. Hebb used the term "deterioration" frequently, and without definition, to cover a wide variety of phenomena; "deterioration" is not what fluctuated frequently in A.

Cases like that of A., with clean-cut loss of tissue and presumably no other lesions at the time of study, provide opportunity for analysis of mental abnormalities; this is precisely the kind of analysis which should enable us to discard a vague, general term like "deterioration" in favor of learning something specific about its components. It is an error to reverse the process and cover up specific details under the blanket term of "deterioration."

Hebb, evidently considering epilepsy to be at the root of many of the behavioral disturbances shown by postoperative patients, suggested that this was responsible for A.'s fluctuations. A., postoperatively only, did have an occasional grand mal seizure with increased irritability for a day preceding the attacks.[5] No evidence of epilepsy appeared in the electroencephalogram of 1940.

Hebb dismissed the case of A. with the statement: "The case is that of a deteriorated epileptic patient with a large removal of the frontal lobes but, also, with an unknown degree of pathologic destruction in the rest of the brain." To classify A. as a deteriorated epileptic is simply incorrect.

The important question is whether the studies made on K. M. were sufficiently thorough to nullify the conclusions of virtually all previous workers; Hebb appeared to believe that they were. Denny-Brown [42] stated that they were not; this is also my opinion. As with a number of other (unilateral) cases in the literature of less critical importance than that of K. M., there is no way to tell, from the data reported, what the postoperative changes may have been. The patient's clinical improvement received most of the emphasis, and there is no careful study of what he may have lost intellectually. The cautions sounded by other workers, Rylander in particular, were not heeded in the studies of K. M. Hebb discarded Rylander's conclusions. The patient's educational, social, and general intellectual status was not taken into account. The psychometric tests were not of a sort to act as a net to catch almost everything, if indeed there are any such tests; and the behavioral data were too few to be very helpful.

STUDIES ON EFFECT OF TOPECTOMY

The observations in cases of lobectomy and lobotomy are considered by the Columbia-Greystone Associates [35] to be useless for the study of frontal lobe function.

41. Hebb,[36] p. 18.

42. Denny-Brown, D.: Frontal Lobes and Their Functions, in Feiling, A., Editor: Modern Trends in Neurology, London, Butterworth & Co., Ltd., 1951.

This opinion depends upon one point, and only that will be discussed. In the topectomies which are the foundation of the book, limited areas of the frontal cortex were removed; the authors found only a few psychological and behavioral changes, and these were not uniform. Hence they expressed doubt that the changes reported by others were really representative of frontal lobe loss. They explained these changes as did Hebb.

The critical point seems to be that removal of small amounts of frontal cortex is in no way comparable to the massive removals dealt with by others. One would expect the changes to be much slighter, if indeed they existed at all, and this is perhaps the major justification for substituting topectomy for lobotomy. Paucity of change after a limited removal in no way reduces the significance of much greater changes after much greater removals.

Critical Evidence.—Indisputable evidence to support one position or the other could come only from (1) patients with (*a*) no preoperative lesion and (*b*) varying amounts of tissue removal, but without anything comparable to the massive destructions of lobotomy, and (2) a thorough comparison of frontal and nonfrontal lobectomies performed for tumor removal.

Patients Without Preoperative Lesion and With Varying Amounts of Tissue Removal: If such patients showed minimal sequelae, or none, after minimal removal of tissue, but typical "frontal lobe symptoms" after more extensive removals, the conclusion would seem inescapable that the symptoms resulted solely from loss of frontal tissue. Contradictory as it may seem, the Columbia-Greystone patients actually seem to be just such a group.

Typical "frontal lobe symptoms" were found after topectomy in three cases; these symptoms the authors themselves attributed to removal of "too much frontal cortex," more than in most topectomies.[35] Of Patient 8 they said (page 415)[35]:

> Postoperative behavior contrasted sharply. Somatic complaints and his self-centered attitude immediately disappeared. He became impulsive; there were great variations in mood. Although generally carefree, garrulous, and outgoing, sudden explosive periods would occur in which he became obstreporous and assaultive. On a few occasions he cut his fist by thrusting it through a window. This and the assaultiveness occurred only in the immediate postoperative period. Remorse did not follow. Marked deterioration in social behavior occurred. He insulted patients and attendants, hoarded prized foods, and demanded special privileges. He was less conscientious in his work. Six months following operation his sister, a nun, visited him. Before operation he had displayed a great respect for her. Now he swore and was so insulting that she found it necessary to shorten her visit. Another relative could not understand his lack of remorse and refusal to apologize. . . .
>
> This patient shows not only the changes in the affective responses, but also exhibits gross deterioration in social behavior. We attribute his lack of concern, absence of tact, and lack of conscientiousness to removal of too much of the frontal lobe. This type of behavior resembles that which we have seen in some our lobotomy patients and is similar to that reported by others to sometimes follow lobotomy.

The Rorschach report[43] disagreed with this clinical statement, saying, among other things, that the patient "became more sociable."

The report on Patient 22 (page 416)[35] follows:

> Three months after operation he was paroled to his home. Although the overt psychotic symptoms were not in evidence, his judgment was quite defective and he lacked his former sense of responsibility. Emotional reactions toward his wife were somewhat unrestrained. Because of lack of education and understanding, and remembering irascible trends that accom-

43. Zubin,[81] p. 286.

panied his previous breakdowns, the patient's wife called the police and he was returned to the hospital. On the ward he remained cooperative without the preoperative impulsiveness, but evidenced, at six months after operation, obvious impairment of judgment and some confusion. Speech was rambling, at times irrelevant, and often centered about remote happenings. This defective judgment had lessened considerably by one year after operation. He was then better oriented on current events, rambled less, and was considered quite responsible by his ward physician. He had ground parole and was free to visit the neighboring village frequently. The ward psychiatrist considered him fit for discharge and felt that the chief impediment to his making a satisfactory social adjustment was his wife's unstable condition. Persistent defective judgment was, however, apparent in this patient's reluctance to live elsewhere than with his wife. Here again the specific alteration of affect occurred and overt psychotic symptoms disappeared, but owing to the removal of too much frontal cortex, deterioration in judgment with irresponsible behavior resulted, making his early return to society impractical. (Note: Just before this was submitted for publication this patient was paroled.)

The Rorschach test was not reported.

Similar postoperative effects occurred with Patient 36 (page 416).[35]

The principal change following operation was the disappearance of remaining agitation and tension. The patient's paranoid development was not markedly changed. Adaptation at home following parole was inadequate, primarily because of indolence and irresponsibility and also because the patient continued to express the persecutory delusions. One year after operation her delusions were unchanged. Behavior on the ward, however, was markedly improved. The ward physician described her as a model patient. When interviewed, she told in detail of the horrible things that people were doing to her but throughout remained in complete equilibrium.

Here, too, the alteration of affective response was achieved and it is necessary to consider two factors in analyzing this patient's failure to adjust adequately. As in the two preceding cases, extensive amounts of cortex were removed, probably accounting for the indolence and tactlessness. Secondly, the regressive reparative processes of the psychosis had gone far, so that affect was largely divorced from ideation. We believe this accounts for persistence of the paranoid picture despite lessened emotions.

The Rorschach report for Patient 36 [44] stated:

After operation she lost her introspective tendencies and was somewhat less rigid but only by sacrificing some degree of maturity in thought and action, since the majority of her inner strivings were reduced to an immature level. She was also less capable of organizing her environment into larger units but the organization that she did effect was a little more tied to reality, and more practical in nature than it was before operation. In general, her receptivity to promptings or strivings from within as well as her receptivity to stimulation from without was not on as mature a level as it was before operation. She showed better contact with reality and responded in a manner indicative of greater communality with her fellows.

Patients 22 and 36 had normal postoperative electroencephalograms. That of Patient 8, who had postoperative grand mal seizures, showed a focal abnormality, but whether it was regular or only preconvulsive is not certain.

The Columbia-Greystone cases are the only ones in the literature without preexisting brain lesions in which "frontal lobe symptoms" have resulted from a relatively limited removal of frontal tissue. Brain distortion and the various factors mentioned by Hebb and Penfield, which can never be excluded in cases of tumor, were nonexistent here. So were the massive destructions incident to lobotomy. Hence, although the symptoms are somewhat sketchily described, these workers seem to have proved that "frontal lobe symptoms" do follow removal of sufficient frontal cortex.

44. Zubin,[31] p. 292.

Comparison of Frontal and Nonfrontal Lobectomies for Tumor Removal: Further conclusive evidence that removal of frontal tissue is the major cause of the behavioral sequelae is to be found in Rylander's series of 16 cases of temporal, occipital, and parietal lobectomies, all performed for the removal of tumors.[45] In contrast to Rylander's findings after frontal lobectomy, these tumor patients showed only "a mild degree of emotional instability, a slight increase in fatigability, a moderate reduction in the power of concentration, and a slight impairment of memory." This contrast, found after exceedingly careful work, is extremely difficult to explain except on the basis of symptoms resulting from frontal lobe loss.

Halstead has contributed similar evidence, after many years of such meticulous work that the results seem indisputable.[46] The details are fully presented in his monograph. Here, it is sufficient to say that Halstead worked out an index of impairment of "biological intelligence," a term covering certain cortical behavioral functions which he considered fundamental. In 26 cases of frontal lobectomy the indices of impairment were about six times as great as those of normal controls and three times as great as those in cases of nonfrontal lobectomy (nine of temporal, five of parietal and four of occipital lobectomy).

RELATION OF AMOUNT OF TISSUE LOSS TO SYMPTOM DEVELOPMENT

The work of the Columbia-Greystone Associates cited above seems to prove a direct relation between the amount of frontal cortex removed and the development of symptoms.

In Rylander's frontal-lobe series, mental changes on the whole showed "a certain tendency toward greater accentuation" in the patients with large excisions.

Newly published work of Speakman and Babkin [47] supports the same probability in cats and dogs. They found increasing symptoms after increasing amounts of frontal lobe removal.

Halstead,[46] on the other hand, found no relation between amount of tissue removed and functional losses as measured by his impairment index.

Lashley's concept of lack of specificity of localization of many processes weaves in and out of such a discussion as this and seems especially applicable to any cerebral function which is essentially additive or logarithmic, as I believe the intellectual function of the frontal lobes to be.

SUMMARY

The brain of A. is described. This patient was the first to have undergone bilateral frontal lobectomy.

Autopsy, 18 years after the intensive clinical studies, revealed new meningiomas. Reasons are given for the belief that these were not present at the time of study.

The supposition of some workers that loss of frontal tissue is not the cause of "typical frontal lobe symptoms" is discussed. The accumulated evidence favors the older idea that such loss is the major cause of the symptoms.

45. Rylander, G.: Mental Changes After Excisions of Cerebral Tissue: A Clinical Study of 16 Cases of Resections in Parietal, Temporal and Occipital Lobes, Acta psychiat. et neurol., Supp. 25, 1943.

46. Halstead, W. C.: Brain and Intelligence: A Quantitative Study of the Frontal Lobes, Chicago, University of Chicago Press, 1947.

47. Speakman, T. J., and Babkin, B. P.: Changes in Behavior Following Frontal Lobectomy in Dogs and Cats, Arch. Neurol. & Psychiat. **63**:433, 1950.

PAIN OF HERPES ZOSTER OPHTHALMICUS

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AND
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HERPES ophthalmicus is one of the commoner forms of herpes zoster (Head [1]). It is usually a disease of adults. Although the acute stage is usually more or less painful, this is rather soon over; and it is the very disagreeable, persistent, painful, burning hyperesthesia of the postherpetic neuralgia which excites the greatest interest. For some mysterious reason, ophthalmic herpes rarely results in postherpetic neuralgia in people under 40 years of age, and the frequency of this most distressing condition tends to increase with age. The pathophysiologic mechanism responsible for the pain of postherpetic neuralgia is unknown, and practically all the various measures which have been tried in an effort to relieve this pain have failed (Sugar and Bucy [2]).

The sensory innervation of the face is well known and so, therefore, are the pathways which presumably might be responsible for this pain. The principal sensory innervation is the trigeminal nerve. In addition, there may be a group of afferent fibers from the face which reach the central nervous system through the sympathetic nerves, ganglia, and rami (Helson [3]; Fay [4]). This possibility warrants consideration, as there is little reason to doubt the existence of such sensory afferent fibers in connection with the sympathetic system elsewhere in the body, notably in connection with the vascular system. We need not be concerned here with the academic discussion as to whether these afferent fibers are to be termed "sympathetic." There is evidence that some of these fibers travel from the face by way of the superior cervical sympathetic ganglion through the cervical sympathetic chain and enter the upper thoracic portion of the spinal cord (Kuntz [5]). Other experimental work has shown the presence of afferent nerves in the carotid plexus of thoracic-spinal and vagal origin which probably extend to the face

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1. Head, H.: Herpes Zoster in a System of Medicine, Edited by C. Alburt and R. D. Rolleston, Ed. 2, London, Macmillan & Co., Ltd., 1910, Vol. 7.

2. Sugar, O., and Bucy, P. C.: Postherpetic Trigeminal Neuralgia, A. M. A. Arch. Neurol. & Psychiat. **65**:131-145, 1951.

3. Helson, H.: The Part Played by the Sympathetic System as an Afferent Mechanism in the Region of the Trigeminus, Brain **55**:114-121, 1932.

4. Fay, T.: Atypical Facial Neuralgia: A Syndrome of Vascular Pain, Ann. Otol. Rhin. & Laryng. **41**:1030-1062, 1932.

5. Kuntz, A.: Autonomic Nervous System, Ed. 3, Philadephia, Lea & Febiger, 1945.

(Kuntz [5]). As these nerves are large and myelinated, Kuntz did not believe that they conduct ordinary pain impulses, and stimulation of the carotid plexus did not evoke pain reactions. The vagus components, however, are nonmyelinated or small myelinated fibers and may conduct pain impulses. Christensen [6] found degeneration in the nasociliary and posterior nasal nerves after section of upper thoracic spinal nerves distal to their dorsal root ganglia, thus giving further evidence of possible afferent fibers to this general area. In addition, some authors have postulated the presence of sensory afferent fibers in the facial, or seventh, cranial nerve and in the motor division of the trigeminal nerve. However, Carmichael and Woolard [7] found no evidence that pain was transmitted by other than fibers of the trigeminal nerve.

The unsatisfactory results from treatment of postherpetic ophthalmic neuralgia have always given rise to doubt as to which of these various afferent pathways were involved. Head and Campbell [8] demonstrated an inflammatory reaction in the sensory ganglia in both the ophthalmic and the spinal form of this disease. Denny-Brown, Adams, and Fitzgerald,[9] in a study of herpes zoster, found not only ganglionitis, but neuritis of the related anterior and posterior roots, and posterior poliomyelitis with neighboring leptomeningitis. Head and Campbell [8] found similar lesions in the brain stem in one of their cases of ophthalmic herpes. However, if the pathologic process is limited to these structures, it is difficult to understand why section of the trigeminal root central to the Gasserian ganglion and section of the spinal root of the trigeminal nerve in the medulla oblongata both fail to relieve the pain. These facts raise the question as to whether the other potential sensory pathways from the face, briefly outlined above, might be concerned in the production of this pain. The following case appears to have important bearing on this point.

REPORT OF A CASE

The patient, a 74-year-old, retired man, was first admitted to the neurosurgical service of the Chicago Memorial Hospital on April 4, 1948, suffering from typical trigeminal neuralgia involving the maxillary division on the right side. These paroxysms of pain had been occurring irregularly over a period of two years. Examination revealed an elderly man with severe generalized arteriosclerosis. His blood pressure was 165/80. The right cornea was scarred as the result of a childhood injury. His hearing was reduced considerably in both ears. On April 5, he was operated upon. The Gasserian ganglion was exposed by the extradural temporal route, and the entire sensory root was divided centrally to the ganglion. The motor root was spared. After the operation, he had the expected total anesthesia of the right side of the face and loss of the corneal reflex. He was free from pain and has continued so ever since. He was discharged from the hospital on the fourth postoperative day.

Second Admission.—After the operation, he had been very well until March 3, 1949, when he struck the right side of his forehead on a door. He felt no pain and paid little attention to the injury, but two days later his sister noted a swelling of his forehead on the right side and two or three marks on that swelling. The following day the right eyelids became swollen. On March

6. Christensen, K.: Innervation of the Nasal Mucosa with Special Reference to Its Afferent Supply, Ann. Otol. Rhin. & Laryng. **43**:1066-1084, 1934.

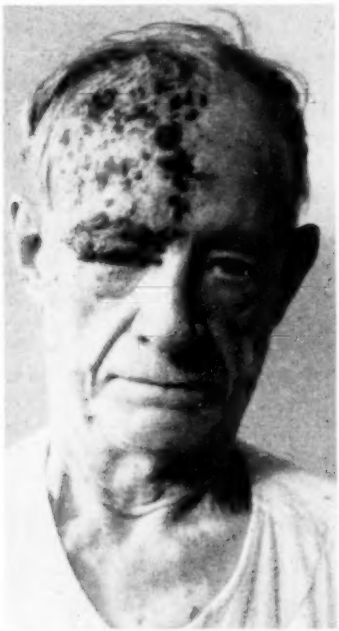
7. Carmichael, E. A., and Woolard, H. H.: Some Observations on the Fifth and Seventh Cranial Nerves, Brain **56**:109-125, 1933.

8. Head, H., and Campbell, A. W.: The Pathology of Herpes Zoster and Its Bearing on Sensory Localization, Brain **23**:353-523, 1900.

9. Denny-Brown, D.; Adams, R. D., and Fitzgerald, P. J.: Pathologic Features of Herpes Zoster: A Note on "Geniculate Herpes," Arch. Neurol. & Psychiat. **51**:216-231, 1944.

9 the forehead and the eyelids became very inflamed. At no time had he suffered any discomfort. On examination, the skin of the right anterior half of the scalp and of the right upper eyelid was found to be swollen, erythematous, and covered with numerous small, macerated, weeping ulcerations. The left eyelids were also slightly edematous. The entire involved area was anesthetic, as was the remainder of the right side of the face; there was an opacity of the right cornea, as before, and the generalized arteriosclerosis was still obvious.

He was seen in consultation with Dr. S. W. Becker, our dermatologist, and Dr. Glenway W. Nethercut, our ophthalmologist. They agreed with us that this patient had severe gangrenous herpes zoster ophthalmicus. Cultures of material from the infected area grew Micrococcus pyogenes var. albus (Staphylococcus albus). The area was treated with nitrofurazone (furacin®) dressings, and penicillin was administered systemically. The condition gradually improved. The



Photograph of patient showing involvement of the skin during the acute phase of the infection.

gangrenous area sloughed, and the granulation tissue then quickly epithelized. The edema soon subsided. He was discharged from the hospital on March 24, two weeks after admission. When he was last seen, over a year after this episode, the lesions were well healed, leaving mottled grayish scars over the right frontal region. At no time, either during the acute infection or afterward, did he suffer from any discomfort or pain.

COMMENT

A thorough search of the literature has revealed no similar case. In a personal communication, Dr. W. J. Gardner, of Cleveland, informed us of a woman in whom ophthalmic herpes zoster developed one year after complete retrogasserian section of the trigeminal nerve for trigeminal neuralgia. She, too, had little or no pain during the acute infection, but two months later complained of a dull, aching pain

in the area of distribution of the second division. The explanation of this pain is in doubt, but obviously it was not postherpetic.

These two cases would seem to establish several facts which are of interest and importance in the consideration of this vexing problem. First, herpes zoster ophthalmicus can occur in an area in which the principal sensory innervation has been severed from the central nervous system between the Gasserian ganglion and the brain stem, but where the skin and the peripheral nerve fibers remain connected to the ganglion cells in the Gasserian ganglion. Second, the pain of acute herpes zoster ophthalmicus is mediated by the trigeminal nerve, and not by any of the other nerves which it has been thought might conduct painful impulses from the face—to wit, the fibers traveling with the sympathetic system, possible sensory fibers from the face traveling over the vagus nerve, or sensory fibers in the facial (seventh cranial) nerve or the motor division of the fifth cranial nerve.

We cannot be equally sure about postherpetic pain, even though it seems likely that a similar statement is true for that condition. Although acute herpes zoster is commonly painful and always uncomfortable (if the sensory innervation has not been severed), this is not true of the postherpetic state. It is true that postherpetic neuralgia usually develops in persons beyond 40 years of age and is commonest in elderly arteriosclerotic persons. Nevertheless, it does not develop in all people even under those circumstances. We cannot, therefore, be certain that either in Dr. Gardner's patient or in ours would postherpetic neuralgia have developed, even if the trigeminal nerves had been intact.

Although these two cases do not solve the problem of the nervous mechanism concerned in the development of postherpetic neuralgia, they do, we believe, rule out peripheral structures other than the trigeminal nerve and cause one to center attention upon central nervous mechanisms.

SUMMARY

The case of a man aged 74 is described. A retrogasserian neurotomy was performed for trigeminal neuralgia, and approximately one year later severe herpes zoster ophthalmicus developed on the same side. This was without pain from the onset and remained so until he was last seen, over a year later.

It is believed that this case demonstrates that the trigeminal nerve is the only peripheral nerve structure which is concerned in ophthalmic herpes—the pain associated with the acute form and probably with postherpetic neuralgia. It shows that the various other pathways, sympathetic, vagal, facial, and motor fifth, which have been cited as possible pathways for painful impulses from the face are not concerned with the pain of ophthalmic herpes, and probably not with postherpetic neuralgia. However, it must still be recognized that section of the trigeminal nerve will not relieve these pains, and that, therefore, the nerve probably serves only as a pathway to the central nervous system and disease in the peripheral nerve is not the cause of the pain once postherpetic neuralgia has developed.

EFFECT OF BREATH HOLDING ON ARTERIAL PRESSURE IN PATIENTS WITH MENTAL AND EMOTIONAL DISORDERS

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THE RELATION of emotion to elevation of arterial pressure has been discussed in the medical literature since essential hypertension was first recognized. Although ample evidence exists that an emotional upset may cause temporary elevation of arterial pressure, there are differences of opinion concerning its importance as the cause of essential hypertension. Among the findings in patients with essential hypertension, as well as in some of their normotensive siblings, is an excessive rise in arterial pressure when carbon dioxide accumulates in the blood during voluntary suspension of breathing.[1] It was therefore considered desirable to study the effect of breath holding on arterial pressure in patients with emotional disturbances. The study also afforded information concerning the reactivity of the vasomotor system in the psychoses studied.

MATERIAL AND METHODS

Seventy-nine patients, of whom 51 were women, were studied by the method of Ayman and Goldshine.[1] The patients were at rest during and for a period prior to the test, but the half-hour pretest rest period recommended by Ayman and Goldshine [1] could not always be enforced. The diagnoses for the patients studied included the common mental and emotional disorders (Chart); 13 of the subjects exhibited diastolic blood pressure levels of 90 mm. Hg or above.

OBSERVATIONS

Increases in systolic and diastolic blood pressure during 20 seconds of breath holding were between 0 and 22 mm. Hg in 77 of 79 patients; in only 2 patients were the rises 23 mm. Hg or more. Changes in arterial pressure were the same in range and distribution in all the diagnostic categories studied.

COMMENT

Patients with essential hypertension regularly exhibit excessive rises in arterial pressure during breath holding [1]; a similar phenomenon occurs in some of their normotensive siblings. The cold-pressor test yields similar increases.[2] Vaso-

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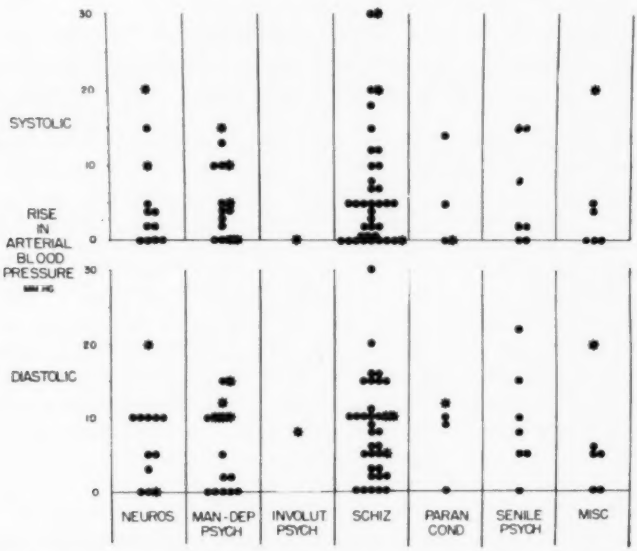
1. Ayman, D., and Goldshine, A. D.: The Breath-Holding Test: A Simple Standard Stimulus of Blood Pressure, Arch. Int. Med. **63**:899, 1939.

2. Hines, E. A., Jr., and Brown, G. C.: The Cold Pressor Test for Measuring the Reactibility of the Blood Pressure: Data Concerning 571 Normal and Hypertensive Subjects, Am. Heart J. **11**:1, 1936. Hines, E. A., Jr.: The Hereditary Factor in Essential Hypertension, Ann. Int. Med. **11**:593, 1937.

motor mechanisms evidently are overreactive to carbon dioxide and to cutaneous stimulation in patients with essential hypertension and in normotensive subjects destined to become hypertensive years later. A similar overreactivity to emotion also occurs in patients with hypertension.[3] It is clear from such studies and from clinical experience that emotion is an important determining factor in the course of essential hypertension.

On the other hand, the present observations, which show no evidence of hyperreactivity during the breath-holding test in patients with various types of emotional disturbance, lend no support to any concept postulating that emotion is the cause



Rise in arterial pressure during breath holding in patients with mental and emotional disorders. Dots represent patients with normal blood pressure; asterisks, patients with hypertension.

of essential hypertension. It is interesting to note in this connection that the cold-pressor test likewise is not abnormal in neuroses [4] or in psychoses.[5] The emotions

3. Palmer, R. S.: The Factor of Mental Stress in Essential Hypertension, New England J. Med. **216**:689, 1937.

4. (*a*) White, B. V., Jr., and Gildea, E. F.: "Cold Pressor Test" in Tension and Anxiety: A Cardiochronographic Study, Arch. Neurol. & Psychiat. **38**:964, 1937. (*b*) Wood, P.: Da Costa's Syndrome (or Effort Syndrome): The Mechanism of the Somatic Manifestations, Brit. M. J. **1**:805, 1941. (*c*) Sullivan, J. D.: Sensory Perception in Hysterical Anesthesia as Measured by the Cold Pressor Response, Arch. Neurol. & Psychiat. **51**:84, 1944. (*d*) Rosen, S. R.: Vasomotor Response in Hysteria, J. Mt. Sinai Hosp. **18**:179, 1951. (*e*) Wolff, H. H.: The Mechanism and Significance of the Cold Pressor Response, Quart. J. Med. **20**:261, 1951.

5. Rosen.[4d] Igersheimer, W. W., and Stevenson, J. A. F.: Effect of Electroshock on the Blood Pressure in Psychotic Patients, A. M. A. Arch. Neurol. & Psychiat. **65**:740, 1951.

described in the case records of the patients studied here were of all types; commonly noted was repressed aggression, which currently is the one most emphasized in psychiatric discussions of essential hypertension.

It has long been known that hypertension is common in psychotic depressions, especially those accompanied by agitation; hypertension is less common in schizophrenia and in manic states. The fact that the breath-holding test does not result in increased blood pressure in psychotic patients with elevated arterial pressure (Chart) suggests that the etiologic agent in hypertension associated with psychoses is different from that of essential hypertension; this hypothesis is supported by the observation that increased arterial pressures associated with psychoses commonly become normal with remission of the psychosis.

The results of the present study show that the vasomotor system, including the center, reacts normally to increased blood-carbon-dioxide concentrations in patients with the emotional and mental disorders discussed here. It is possible that if a full half-hour of rest could have been obtained prior to the test the results might have shown a slightly greater degree of reactivity in that lower control levels might have been found. Even apathetic schizophrenic patients show lowering of arterial pressure with habituation to the measurement of blood pressure.[6] It was pointed out previously that the vasomotor reactions to posture [7] and to temperature [8] are not diminished in schizophrenia. The effects of the injection of sympathomimetic and parasympathomimetic drugs have been interpreted erroneously as providing evidence concerning the reactivity of the autonomic nervous system. Such studies afford information in regard to (*a*) the reactivity of the end-organs, that is, the blood vessels and heart, and not the nerves going to them, and (*b*) the effectiveness of enzyme systems that inactivate these drugs. There is no physiologic evidence that the sympathetic nervous system is underresponsive in schizophrenia or in other mental disorders.

SUMMARY AND CONCLUSIONS

The effect of breath holding on arterial pressure in patients with severe neuroses or with manic-depressive, involutional, schizophrenic, or senile psychoses is the same as its effect in normal persons. The amount or nature of emotional activity of the brain does not influence the results of the breath-holding test. There is no physiologic evidence that the amount and nature of emotional activity of the brain are important in causing essential hypertension, although clinical experience indicates that emotion may influence the course of that disease. The reactivity of the vasomotor mechanisms to increased blood-carbon-dioxide concentration is normal in the mental conditions discussed here.

6. Freeman, H.: Effect of "Habitation" on Blood Pressure in Schizophrenia, Arch. Neurol. & Psychiat. **29**:139, 1933.

7. Altschule, M. D., and Lorenz, M.: Observations of Nitrite-Induced Postural Syncope in Patients with Mental Disease, Proc. Soc. Exper. Biol. & Med. **71**:6, 1949.

8. Altschule, M. D., and Sulzbach, W. M.: Effect of Carbon Dioxide on Acrocyanosis in Schizophrenia, Arch. Neurol. & Psychiat. **61**:44, 1949.

FURTHER STUDIES ON THE IRON CONTENT OF THE CEREBROSPINAL FLUID IN PSYCHOSES

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AND
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IN A PREVIOUS paper,[1] the results of a study on the iron content of the cerebrospinal fluid of 98 patients committed to a mental hospital were reported. After the patients had been divided into various diagnostic groups, a statistically significant difference between the spinal-fluid iron of the patients with acute schizophrenia and that of the deteriorated schizophrenic patients appeared. It was found, furthermore, that the difference between the iron content of the fluid of nondeteriorated schizophrenic patients and that of the patients with organic disease was highly significant, whereas no significant difference could be found between the organic group and the deteriorated schizophrenic patients.

On the basis of this study and of the data collected from the literature, it was assumed that a low iron content of the spinal fluid is indicative of increased brain metabolism and that high iron values for the spinal fluid may reflect reduced cellular activity of the brain tissue.

Since the completion of our first study, we have continued the investigation along several lines. Our case material in the various diagnostic groups has been increased. The problem of the relative constancy of the values for the spinal-fluid iron has been studied. Finally, an attempt has been made to induce experimental changes in the spinal-fluid iron by the intravenous administration of iron.

The quantitative determination of the spinal-fluid iron was done by the same method as that described in our previous publication. Essentially the same method was used for the determination of the serum iron, with only minor modifications in the digestion of the same made to take into account the extra protein.

RESULTS ACCORDING TO DIAGNOSTIC CATEGORIES

The new material used in the present series comprised 36 spinal fluids derived from 29 patients. After classification of these patients according to the system used in our previous study, the results shown in Table 1 were obtained.

From the Verdun Protestant Hospital.

Miss Dorothy K. Turnbull, M.Sc., performed the chemical analyses. Dr. G. E. Reed, medical superintendent of the Verdun Protestant Hospital, gave permission for the publication of this report.

1. Lehmann, H. E., and Kral, V. A.: Studies on the Iron Content of Cerebrospinal Fluid in Different Psychotic Conditions, A. M. A. Arch. Neurol. & Psychiat. **65**:326-336, 1951.

Because of the small number of patients in this series, no detailed statistical evaluation was attempted. However, the main results obtained are in keeping with our previous findings. The mean for the whole new material was found to be 0.043 mg. per 100 ml.; in our first study, it was 0.042 mg. per 100 ml.

In our nonpsychotic group (comprising one patient with psychopathic personality and four mentally deficient persons) the range of spinal-fluid iron was found to lie between 0.014 and 0.080 mg. per 100 ml., with a mean of 0.040 mg. per 100 ml. In the previously reported material, the mean was 0.038 mg. per 100 ml. In the organic group, comprising 16 patients (11 patients with dementia paralytica, 3 with presenile dementia, and 2 with epilepsy) the spinal-fluid iron ranged from a trace

TABLE 1.—*Diagnostic Classification and Statistical Data of New Material*

Group	No. of Cases	No. of Spinal Fluids	Range, Mg./100 Ml.	Mean Iron in Mg./100 Ml.
Nonpsychotic	5	6	0.014-0.080	0.040
Organic psychoses	16	19	Trace-0.095	0.043
Schizophrenic, nondeteriorated	4	7	Trace-0.058	0.031
Schizophrenic, deteriorated	3	3	0.037-0.075	0.055
Schizophrenic, whole group	7	10	Trace-0.075	0.041
Miscellaneous	1	1	0.062	.....
Total	29	36	Trace-0.095	0.043

TABLE 2.—*Diagnostic Classification and Statistical Data of Old and New Material Combined*

Group	No. of Cases	Range, Mg./100 Ml.	Iron in Mg./100 Ml., Mean	Standard Deviation
Nonpsychotic	23	0.005-0.093	0.039	0.022
Organic	49	Trace-0.095	0.045	0.024
Schizophrenic, nondeteriorated	23	Trace-0.058	0.032	0.015
Schizophrenic, deteriorated	14	0.017-0.075	0.048	0.017
Schizophrenic, whole group	37	Trace-0.075	0.038	0.017
Miscellaneous	14	0.011-0.090	0.048	0.024
Total	123	Trace-0.095	0.042	0.022

to 0.095 mg. per 100 ml., with a mean of 0.043 mg. per 100 ml. In this group the mean was lower than in the first series, where it was found to be 0.047 mg. per 100 ml. This small difference may be due to our selection of patients with organic disease, which this time did not include any cases of Parkinsonism, a condition which has been shown to be associated with particularly high iron values of the spinal fluid.

Most interesting were the findings in the schizophrenic group. The mean value of the spinal-fluid iron for our new group of seven schizophrenic patients was 0.041 mg. per 100 ml. This value is somewhat higher than the mean for the previously reported series, which was 0.037 mg. per 100 ml. This difference, however, may result from the unusually high iron values for three deteriorated patients included in this group. The mean iron value for this deteriorated subgroup was 0.055 mg. per 100 ml., whereas the mean value for the nondeteriorated schizophrenic patients was 0.031 mg. per 100 ml.

Although our new schizophrenic material is small, the values emphasize the previous finding that the spinal-fluid iron tends to be considerably higher in the deteriorated than in the nondeteriorated schizophrenic patients.

In view of the similar profile of trends and the similarity of the method employed for the selection of patients, we felt justified in adding our new results to the old ones and in considering the total of 103 patients. Table 2 presents the data for the two investigations combined.

CONSTANCY OF SPINAL-FLUID IRON

Another aim of the present study was to determine whether the iron content of the spinal fluid remains fairly constant or whether it is subject to fluctuations and, if so, what factors may be responsible for these variations. For this purpose, 35 spinal fluids were reexamined, some of them several times, giving a total of 39 follow-up samples. The time interval between the original and the second or third examination varied from less than 24 hours to almost 2 years.

The crude results of these 39 reexaminations were as follows: The iron content was found to be identical on reexamination in only one spinal fluid. Sixteen spinal fluids showed an increase in the iron content. A decrease of the iron content was found in 22 spinal fluids. Of those instances in which reexamination was performed more than once, a constant increase of the spinal-fluid iron was found in two, a constant decrease in one, and an increase followed by a decrease in one.

However, an examination of these figures statistically yields the following results: In 34, or 87%, of the spinal fluids studied the difference between the first and the second value was found to lie in the range of twice the standard deviation, 0.022. In five reexaminations (13%) the differences in the two values for the iron content exceeded twice the standard deviation.

We examined the factors of age, sex, and time lapse between the examinations as possible causes of the fluctuations in the spinal-fluid iron which appeared in our reexaminations. A statistical analysis of our data by the chi-square method revealed only the time factor to be significantly related to the changes. In 14 instances in which the reexamination was performed within six months no change of a magnitude greater than twice the standard deviation had occurred. Of 25 instances in which reexamination was performed after more than six months a change of greater than twice the standard deviation occurred in 20%.

We had anticipated a correlation of the sex of the patients and the constancy of the spinal-fluid iron, since it was thought that loss of iron associated with the menstrual hemorrhages in women might have influenced the iron in the spinal fluid. This was found not to be true. Age was also found to be unrelated to changes in values for the spinal-fluid iron.

It was noted that of 10 originally, nondeteriorated schizophrenic patients, 2 showed a difference in the values of spinal-fluid iron exceeding twice the standard deviation. Both had an increase of their spinal-fluid iron, and, as one might have expected, both presented the picture of progressive deterioration.

EXPERIMENTAL INCREASE OF SPINAL-FLUID IRON

The last phase of this investigation was concerned with the question whether, and to what extent, the iron content of the spinal fluid could be changed by the intravenous injection of iron. The preparation used was "feojectin," a saccharated iron oxide containing 2% iron. Iron in this form was employed by Cameron, Bensley, Wood and Grayston,[2] who reported that it produced no untoward side-effects, even if administered by the intravenous route.

The following method was generally followed: A lumbar puncture was performed in the morning for determination of the spinal-fluid iron. Immediately after the lumbar puncture, 100 mg. of "feojectin" was slowly injected into the vein. After an interval of 30 minutes, and again after 6 hours, spinal punctures were done for determination of the spinal-fluid iron. In a few cases the timing of the lumbar punctures was slightly changed: In two cases additional lumbar punctures were performed after three hours, so that these two patients had four lumbar punctures, one before and three after administration of "feojectin." In two cases the lumbar puncture 30 minutes after the injection was omitted and a 3-hour puncture substituted. In two cases an additional lumbar puncture was performed 24 hours after the "feojectin" was given. In seven cases the iron content of the serum was determined parallel with each determination of the spinal-fluid iron. It should be mentioned that we did not observe the slightest untoward side-effect resulting from the iron administration.

TABLE 3.—*Changes in Spinal-Fluid Iron Following Intravenous Injection of 100 mg. of "Feojectin"*

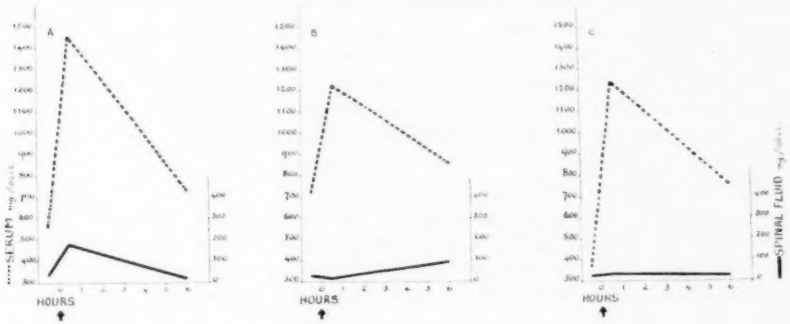
		Iron Content, in Mg./100 Ml.		
		Before	30 min. After Injection	6 Hr. After Injection
Serum	Range	0.14-0.72	0.60-1.45	0.32-0.91
7 cases	Mean	0.42	1.17	0.63
Spinal fluid	Range	Trace-0.080	0.010-0.300	0.014-0.200
18 cases	Mean	0.028	0.061	0.063

The results of our observations are given in Table 3. This Table shows clearly that the serum iron, which was approximately 10 to 20 times as high as the spinal-fluid iron, rose far above the original value during the first half-hour after the intravenous injection of 100 mg. of "feojectin." On the average, this increase reached nearly 300% of the original value. Most important is the fact that this increase in the serum iron during the first half-hour occurred without exception in every case. These observations are in keeping with the findings of Cameron and associates, who observed a considerable increase in the serum-iron content during the first five minutes after an injection of 40 to 200 mg. of "feojectin."

The spinal-fluid iron behaved somewhat differently after the administration of 100 mg. of "feojectin." In the first 30 minutes after the injection, we found an

2. Cameron, D. G.; Bensley, E. H.; Wood, P., and Grayston, V.: Treatment of Iron Deficiency Anaemia with Saccharated Iron Oxide by the Intravenous Route, Canad. M. A. J. **64**:27-30, 1951. Cameron, D. G.; Bensley, E. H., and Wood, P.: Some Effects of Intravenous Injections of Saccharated Iron Oxide on Serum Iron and Unsaturated Iron Binding Capacity, ibid. **64**:31-32, 1951.

increase in the mean iron content of the spinal fluid amounting to about 100% of the original value. This was due to the magnitude of the individual increase, which, when it occurred, varied from 100 to 600% of the original level. However, such an increase 30 minutes after the injection was found in only 6 of 16 patients. Ten patients had either no increase at that time or one not statistically significant. Six hours after injection of "feojectin" the mean value for spinal-fluid iron was unchanged as compared with the mean 30-minute value; that is, it was about twice as high as the original value. At that time 11 of 18 patients showed a value for iron significantly higher than the original level. However, a detailed study of the individual patients revealed a different behavior. In three of the six patients who showed increased spinal-fluid iron 30 minutes after the injection the spinal-fluid iron had returned to the level of the original value; in one it had remained unchanged, and in two a further increase had occurred. Of the 10 patients who had no increase in spinal-fluid iron 30 minutes after injection, 5 did not have an increased iron



A, early rise of spinal-fluid iron, corresponding with increase of serum iron; *B*, late rise of spinal-fluid iron; *C*, no rise of spinal-fluid iron.

value six hours after administration of "feojectin," whereas the other 5 did. Again, this increase varied considerably in amount.

Of the two patients on whom determination of iron was performed 24 hours after the administration of "feojectin," in addition to the regular schedule, one showed still the same level as that three hours after injection, the latter apparently representing the maximum rise. In the other patient the spinal-fluid iron had receded from a maximum, at six hours, to the original level at 24 hours.

Taken together, our observations showed that of 18 patients studied, 13 exhibited an increase in spinal-fluid iron content after the injection of 100 mg. of "feojectin." Five patients did not show any increase during the observation period. On 3 of the latter parallel determinations of the serum iron were performed and showed a considerable rise. Of the 13 patients with an increase of spinal-fluid iron, 6 exhibited that increase during the first 30 minutes. In seven it took place only after a long interval, varying from three to six hours.

The Figure illustrates these three types—early and late reactors and nonreactors.

Analysis of our data showed that increase or failure of the spinal-fluid iron to increase was not dependent on the original, preinjection level of iron in the serum or the spinal fluid, nor was it dependent on the sex, age, or diagnostic category of the patient.

COMMENT

The clinical significance of the iron content of the spinal fluid which emerges from the statistical analysis of our first series of 98 patients has been confirmed by findings in this new series of 29 patients. Again, it appears that the mean value for the iron content of the spinal-fluid in a group of patients with organic psychoses is higher than that for subjects without psychoses. Further confirmation was found in this investigation for the interesting finding that the clinical dichotomy between deteriorated and nondeteriorated schizophrenic patients is reflected in the iron content of their spinal fluid. In our previous publication, we arrived at the theoretical assumption that there may exist an inverse relation between cellular activity in the brain and the iron content of the spinal fluid. Judging from the iron levels of the spinal fluid, it would appear that a significant similarity exists between metabolic processes in the brain of patients with organic cerebral damage and patients presenting the clinical picture of schizophrenic deterioration.

The relative constancy of values for iron in the spinal fluid has been demonstrated by the results of repeated iron determinations in 35 cases. Redeterminations were done within periods ranging from 24 hours to 24 months, the average time lapse being approximately 10 months. In 87% of the cases values for iron were within the range of twice the standard deviation. For the five cases (13%) in which changes in the amount of iron exceeded twice the standard deviation, no adequate explanation can be given. We assume that factors involving changes in cerebral metabolism were responsible for the differences found in the iron values. These metabolic changes may have been temporary fluctuations, which were not necessarily represented in a change in the clinical picture. It should be noted, however, that two schizophrenic patients who showed a significant increase of iron in the spinal fluid over a period of a year also showed progressive deterioration of the psychiatric status.

One object of this investigation was to determine whether, and to what extent, this relatively stable level of iron in spinal fluid could be altered by a sudden increase of iron in the circulating plasma.

Italian workers,[3] investigating the changes in the iron level of the blood following intravenous administrations of bivalent and trivalent iron (ferro-calcium [iron-calcium gluconogalactogluconate]; ferronascin) in amounts equivalent to approximately 7 mg. of iron, observed that the maximum value was usually reached after 30 minutes and that the 4-hour value was, as a rule, still elevated. In their material appeared distinct differences with regard to the speed and magnitude of iron clearance in the blood when patients with acute schizophrenia were compared with patients with chronic disease. In their patients with chronic schizophrenia, the values for blood iron reached higher levels and remained high longer than values in their control group. Their patients with acute schizophrenia, on the other hand, had

3. Ferroni, A., and Lipani, G.: Curve sideremiche da carico in amenti e schizofrenici, Acta neurol. **3**:568, 1948. Indovina, I., and Ferroni, A.: Curve sideremiche da carico nel parkinsonismo da encefalite, ibid. **2**:891, 1947.

lower basal levels and a flatter iron clearance curve than did the control material. In a group of patients with postencephalitic Parkinsonism, the findings for blood iron were similar to those for patients with acute schizophrenia, that is, lower basal levels and a lower curve than in the control group, although, according to the same authors [4] and to our own findings, the spinal-fluid iron in patients with Parkinsonism is usually elevated.

In our material, the iron content of the serum rose significantly in each of seven patients, reaching its maximum in 30 minutes after an intravenous injection of saccharated iron oxide ("feojectin"). Of 18 patients who received an injection of the same iron compound, 13, that is, approximately 72%, showed an increase of the iron content of the spinal fluid, although it must be assumed that in all of them the serum iron had been increased. About half the patients in whom an increase of spinal-fluid iron could be demonstrated showed this reaction within 30 minutes. In the other half the spinal-fluid iron was not affected for from three to six hours. An examination of factors which could possibly be responsible for this difference in the neurochemical behavior of different subjects did not produce any clue, since, age, sex, clinical condition and basal iron content of the spinal fluid were not related to behavior of the spinal-fluid iron following an intravenous injection of iron.

It has been pointed out previously that two sources of the spinal-fluid iron must be considered, the blood and the brain. The relative significance of the two sources is not yet clear. It is well known,[5] however, that the passing of a substance from the blood into the spinal fluid is dependent on several factors: the chemical and physicochemical characteristics of the substance in question, the level of concentration achieved, its persistence in the plasma for a sufficient length of time, and the functional status of the barrier, particularly its permeability in either direction. The final concentration of a substance in the spinal fluid is, of course, determined by still another factor—the metabolic processes involving the substance in question within the cerebrospinal-fluid cavity.

We have to consider the possibility that in those of our cases in which we could not demonstrate an increase of the spinal-fluid iron after raising experimentally the iron level in the plasma, we may have missed a transitory increase in the spinal-fluid iron. Other possibilities seem more probable, namely, the influence of different degrees of permeability of the barrier and of individual deviations of the iron metabolism in the cerebrospinal cavity.

Since we were not primarily interested in the functional state of the barrier between the blood and the spinal fluid, no systematic experiments were carried out in this direction. Our patients, however, belonged to different diagnostic groups, some of which are known to be associated, in most cases, with an increased permeability of the barrier, while in others no such disturbance in the permeability of the barrier is usually found. Our results lend support to the assumption that the permeability of the barrier in itself is not of decisive influence, for there was an approximately equal number of cases of all diagnostic groups among those in which the spinal-fluid iron was not increased and among those in which there was

4. Ferroni, A., and Indovina, I.: Ferro labile nel siero e nel liquor nel parkinsonismo, Boll. Soc. med.-chir. Catania **13**:271, 1945.

5. Katzenelbogen, S.: The Cerebro-Spinal Fluid and Its Relation to the Blood: A Physiological and Clinical Study, Baltimore, Johns Hopkins Press, 1935.

an early or a late increase. We believe, therefore, that the metabolic processes within the cerebrospinal-fluid cavity—the active absorption, retention, and secretion of iron—are of decisive importance in establishing the level of iron in the spinal fluid, even after the intravenous injection of iron. This point awaits further clarification through the use of other substances for testing the permeability of the barrier simultaneously with the determination of iron in the blood and in the spinal fluid. At present, there are grounds for the assumption that the passing of iron from the blood into the spinal fluid is determined to a large extent by the iron metabolism in the cerebrospinal-fluid cavity, probably in the nerve tissue itself.

SUMMARY

1. The iron contents of the cerebrospinal fluid of 29 patients belonging to previously established categories were determined.

2. The constancy of the iron level in the cerebrospinal fluid was examined with regard to the factors of time, age, sex, and clinical status.

3. The response of the cerebrospinal-fluid iron to an intravenous injection of 100 mg. of "feojectin" (saccharated iron oxide) was studied, and various types of reaction were described.

COMMUNICATING HYDROCEPHALUS FROM DIFFUSE MENINGEAL TUMOR

Report of Two Cases with Increased Intracranial Pressure Treated by Use of Polyethylene Tube

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THIS REPORT was prompted by the circumstance that both the patients reported had unusual clinical histories and that in both communicating hydrocephalus developed as a result of meningeal meningiomatosis. In addition, attempts were made to control the increased intracranial pressure in each instance by the use of drainage through a polyethylene tube. The character of the lesions was not revealed until necropsy. Necropsy also afforded an opportunity to study the effects of the various operative procedures which had been employed in the hope of controlling increased intracranial pressure and the communicating hydrocephalus.

It is not within the scope of this presentation to discuss the cause of hydrocephalus [1] or the merits or demerits of procedures employed in attempting to control hydrocephalus of the obstructive [2] or communicating type.[3] Russell [4] discussed the pathologic changes in this condition, and Davidoff [5] reviewed the literature con-

† Dr. Adson died Nov. 12, 1951.

From the Section of Neurologic Surgery (Drs. Adson and Dodge) and the Section of Pathologic Anatomy (Dr. Kernohan).

1. Dodge, H. W., Jr.; Svien, H. J., and DuShane, J. W.: Arrested Hydrocephalus: Report of Case, Proc. Staff Meet., Mayo Clin. **25**:518-522 (Aug. 30) 1950.

2. Svien, H. J.; Love, J. G.; Dodge, H. W., Jr., and Keith, H. M.: Evaluation of "Seton" Procedure in the Treatment of Infantile Communicating Hydrocephalus, J. Pediat. **40**:298-302 (March) 1952.

3. Dandy, W. E.: Extirpation of the Choroid Plexus of the Lateral Ventricles in Communicating Hydrocephalus, Ann. Surg. **68**:569-579 (Dec.) 1918. Putnam, T. J.: Results of the Treatment of Hydrocephalus by Endoscopic Coagulation of the Choroid Plexus, Arch. Pediat. **52**:676-685 (Oct.) 1935; Surgery of Infantile Hydrocephalus, Surgical Treatment of the Nervous System, Philadelphia, J. P. Lippincott Company, 1946. Scarff, J. E.: Endoscopic Treatment of Hydrocephalus; Description of Ventriculoscope and Preliminary Report of Cases, Arch. Neurol. & Psychiat. **35**:853-861 (April) 1936.

4. Russell, D. S.: Observations on the Pathology of Hydrocephalus, Medical Research Council, Special Report Series, No. 265, London, His Majesty's Stationery Office, 1949.

5. Davidoff, L. M.: Treatment of Hydrocephalus: Historical Review and Description of a New Method, Arch. Surg. **18**:1737-1762 (April) 1929.

cerning various operative methods of treatment. Ingraham and associates,[6] Matson [7] and Nosik [8] have offered new methods of shunting excessive cerebrospinal fluid into either the ureter or the antrum of the middle ear.

Communicating hydrocephalus results from faulty circulation or absorption of cerebrospinal fluid.[9] The commonest cause is low-grade leptomeningitis. Occasionally leptomeningitis with adhesions develops as the result of subarachnoid hemorrhage. Communicating hydrocephalus sometimes becomes stationary. The reason for this arrest is not clearly understood, but it is probably due either to improvement in the absorbing mechanism or to development of a balance between the secretory and absorbing mechanisms.[10]

The clinical history of both these patients suggested that the symptoms may have been initiated by the presence of low-grade leptomeningitis. In both there was evidence of increased intracranial pressure without definite neurologic signs of a cerebral neoplasm.

REPORT OF CASES

CASE 1.—A married white man, aged 21, was registered at the Mayo Clinic and admitted directly to the hospital on Feb. 17, 1949. He had been well until November, 1948, when he noted fever, general malaise, pains in the muscles, and stiff neck. His physician suspected that he had poliomyelitis. Recovery was gradual until the middle of December, 1948, when the patient had a second attack, at which time he complained of double vision and frequent headaches. The headaches occurred two or three times a week, were worse in the evening than during the day, and were frequently relieved when the patient was recumbent or when he slept. Four days before admission he experienced a third attack, characterized by severe headache, high fever, a state of confusion, and alternate periods of stupor and levity.

Examination revealed that the patient was obviously ill. The pulse rate was 68 per minute, and the blood pressure was 124 mm. Hg systolic and 76 mm. diastolic. The general physical condition was otherwise normal.

Neurologic examination revealed confusion, disorientation, and euphoria. The patient was uncooperative. There was no nuchal rigidity. The objective neurologic status was otherwise normal. Examination of the optic fundi disclosed bilateral papilledema of 4 D., and measurement of the perimetric fields during the patient's more lucid intervals revealed only enlarged blind spots.

Electroencephalogram showed a focus of delta waves, Grade 1, located over the right posterior parietal region. Laboratory examination of the blood showed 14.6 gm. of hemoglobin per 100 cc. Roentgenograms of the skull revealed marked erosion of the floor of the sella turcica and of the dorsum sellae turcicae, presumably as a result of the increased intracranial pressure.

The differential diagnosis included meningoencephalitis, leptomeningitis, and a tumor in the posterior fossa.

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6. Ingraham, F. D.; Matson, D. D.; Alexander, E., Jr., and Woods, R. P.: Studies on the Treatment of Experimental Hydrocephalus, J. Neuropath. & Exper. Neurol. **7**:123-143 (April) 1948.

7. Matson, D. A.: A New Operation for the Treatment of Communicating Hydrocephalus: Report of a Case Secondary to Generalized Meningitis, J. Neurosurg. **6**:238-247 (May) 1949.

8. Nosik, W. A.: Ventriculomastoidostomy: Technique and Observations, J. Neurosurg. **7**:236-239 (May) 1950.

9. Torkildsen, A.: A New Palliative Operation in Cases of Inoperable Occlusion of the Sylvian Aqueduct, Acta psychiat. & neurol. **14**:221, 1939.

10. Weed, L. H.: Studies on Cerebro-Spinal Fluid: II. The Theories of Drainage of Cerebro-Spinal Fluid with an Analysis of the Methods of Investigation, J. M. Research **31**:21-49 (Sept.) 1914; III. The Pathways of Escape from the Subarachnoid Spaces with Particular Reference to the Arachnoidal Villi, ibid. **31**:51-91 (Sept.) 1914; IV. The Dual Source of Cerebro-Spinal Fluid, ibid. **31**:93-117 (Sept.) 1914.

A pneumoencephalogram revealed slight dilatation but no shift of the ventricular system, and there was no evidence of a tumor mass.

Laboratory examination of the cerebrospinal fluid revealed 160 mg. of protein per 100 cc.; 6 lymphocytes per cubic millimeter, and 699 mg. of chloride and 65 mg. of sugar, per 100 cc. A Kolmer test done on the cerebrospinal fluid gave normal results.

On the basis of these findings, it was believed that the patient had a communicating hydrocephalus, which was probably postinflammatory. After a few days of dehydration therapy, he was sent home with instructions to limit the intake of fluids, to have his eyes examined, and to have roentgenograms of the skull in one month.

The dehydration regimen produced initial improvement in the patient's condition. However, after the first week at home he began to experience blurring of his vision and intermittent frontal headaches.

One month after returning home he awakened one morning complaining of severe headache, and during the next few days he noticed rapid loss of visual acuity. He was lethargic, felt very tired, and was content "just to lie around." His physician advised him to return to the clinic for further evaluation and treatment.

When the patient was readmitted to the hospital, neurologic examination revealed him to be drowsy and confused but did not disclose any localizing neurologic signs. Fundoscopy showed bilateral papilledema of 6 D., and visual acuity was found to be so reduced that the patient could perceive only light. Roentgenograms of the skull revealed evidence of increased intracranial pressure.

A subtemporal decompression was performed on March 29, 1949, and treatment by means of dehydration and daily drainage of cerebrospinal fluid was begun.

Three weeks later vision had improved to 14/224 on the right and 14/141 on the left, and the papilledema had receded to 2 D. For facilitation in the reduction of papilledema, drainage by means of a silk seton placed in the lumbar subarachnoid space was instituted.

After this procedure the tissues overlying the region of the subtemporal decompression remained flat; the patient was alert and felt well, and his vision improved, so that once again it was considered safe to allow him to return home.

This state of well-being continued for two weeks, at which time the patient suddenly lost his appetite. The following day it was noted that the scalp overlying the subtemporal decompression was beginning to bulge. Because of frequent vomiting and a semistuporous appearance, he was again hospitalized. Examination disclosed dysarthria and semicoma. Neurologic examination showed hyperreflexia and a Babinski sign on the left side. The tissues over the site of subtemporal decompression were bulging prominently. Moderate stiffness of the neck was noted, and the Kernig and Lasègue signs were both present. Visual acuity was recorded as 14/89 in each eye, and the fields were uniformly contracted. There was bilateral papilledema of 4 D. Examination of cerebrospinal fluid removed by means of spinal puncture at this time revealed a value for protein of 1,000 mg. per 100 cc. and 1 lymphocyte per cubic millimeter.

Since the patient was again experiencing acute hydrocephalus, a left ventriculomastoidostomy was performed on May 10. The immediate postoperative course was uneventful. The region overlying the site of subtemporal decompression became flat and then depressed. The patient was alert and well oriented and had a good appetite. Neurologic examination gave normal results except for the presence of bilateral papilledema of 2 D. Patency of the ventriculomastoid shunt was determined by having the patient lean forward. This maneuver caused copious drainage of cerebrospinal fluid from the patient's nostrils.

Ten days later the patient had made such good recovery, and the shunt was obviously functioning so well, that it was decided to allow him to return home again.

At home the patient found that he was easily able to read a newspaper. He could drive his car, and he had gained 30 lb. (13.6 kg.). He had been instructed to check constantly the status of his shunt, either by palpating the scalp overlying the site of the right subtemporal decompression or by leaning forward to obtain drainage of cerebrospinal fluid from his nose.

On June 15, 1949, evidences of drainage suddenly ceased. During the next few days the patient noticed that his vision was failing. On June 22, he began to vomit, became confused, and noted that the tissues over the site of the decompression were once again bulging. He became increasingly drowsy, and it was deemed necessary once again for him to return to the hospital.

Examination on the day of admission, July 2, revealed the patient to be drowsy, disoriented, and confused. There was prominent bulging over the site of decompression, and he displayed stiffness of the neck. Immediate spinal puncture was performed, and the pressure of the cerebrospinal fluid was found to be 60 cm. of water. A catheter was inserted into the lumbar subarachnoid space on July 5 in an attempt to provide continuous drainage. The patient improved remarkably after drainage of cerebrospinal fluid. However, after 1½ days, the spinal catheter ceased to function, and the patient's condition once again became critical. Insertion of a polyethylene tube to establish drainage of cerebropsinal fluid from the lumbar subarachnoid space to the peritoneal cavity was done on July 12.

The patient's convalescence was uneventful. The fluid intake was limited to 1,500 cc. a day for two days, after which it was raised progressively to 2,000 cc., then to 2,500 cc., and finally to 3,000 cc. a day.

On the morning after operation the scalp over the site of subtemporal decompression was soft and flat, and by the following evening it was beginning to be depressed. The patient displayed mental alertness, a feeling of well-being, and return of his appetite. His wounds healed by first intention, and the sutures were removed on the eighth day. It was noted that each morning the site of decompression bulged slightly or lay flush with the skin; however, as soon as the patient assumed an erect position, the site became depressed. Repeated neurologic examinations failed to show any evidence that the operative procedure or the presence of the plastic tube in the lumbar subarachnoid space caused any irritation or damage. There was no tenderness of the abdomen or over the liver. The bowels and bladder functioned normally throughout the convalescence. Fundoscopic examination on July 19 revealed for the first time the absence of papilledema. Vision had improved to 14/42 on the right and 14/89 on the left.

The patient was dismissed from the hospital July 27. He was ambulant, had gained weight, had a good appetite, but was still weak if he remained up for any length of time. Three weeks after the operation the site of decompression was retracted, and, except for easy fatigue and weakness, the patient's progress was satisfactory. In the first part of August, 1949, he was able to take moderately long automobile rides and to remain erect for increasingly longer periods. It was noted in August that when he was in bed the site of subtemporal decompression bulged slightly or remained flush with the skin and that it pulsated gently. Whenever the patient stood erect, however, the site of decompression became depressed.

At the end of the second week in August, the patient complained of headache, noted slight paresis of the muscles supplied by the sixth cranial nerve on the left, and experienced nausea with occasional vomiting. The site of decompression remained. On the assumption that excess drainage of fluid from the subarachnoid space was occurring, the physician prescribed intake of fluid in large amounts, increased intake of salt, and a diet high in calories, protein, and vitamins. At no time did the patient have any abdominal distention, pain, or tenderness. Both the bowels and the bladder functioned well. After Aug. 15 he became slightly confused, although apparently adequate drainage of the subarachnoid space persisted, as evidenced by retraction of the site of the decompression when the patient was erect. In addition, nausea and vomiting occurred; the paresis caused by involvement of the sixth cranial nerve on the left side became more pronounced, and the patient complained of photophobia. Two days later a series of attacks of Jacksonian epilepsy occurred which involved the right side of the face and the right arm. These were followed by severe attacks of grand mal, which usually started in the right arm and the right side of the face. The frequency of these attacks rapidly increased until status epilepticus supervened.

On Aug. 17, 1949, the patient was admitted to the hospital for the fifth time. On admission he had a rectal temperature of 100 F., a pulse rate varying from 100 to 110 per minute, and erratic respirations. The seizures were controlled by intravenous administration of barbiturates. He was placed in an oxygen tent; a Magill airway was inserted, and intravenous administration of fluids was started. Penicillin was also administered.

Improvement in the patient's general condition gradually took place, so that by the next evening he was responding moderately well. Neurologic examination at this time showed paralysis, graded 1 to 2, of the left lateral rectus muscle, gross nystagmus in all directions, and slight upward deviation of the eyes. There was no nuchal rigidity, and the Babinski sign could not be elicited. The site of decompression remained flat. Anticonvulsant therapy was continued.

Blood electrolytes were normal. However, in spite of all treatment, the patient gradually became drowsy and responded poorly. He became progressively worse and died Aug. 30, 1949.

Necropsy disclosed the presence of 350 cc. of clear yellow fluid in the peritoneal cavity. A polyethylene tube located between the liver and the diaphragm projected 1 cm. into the peritoneal cavity at the level of the 12th rib. There was no peritoneal reaction. The polyethylene tube was patent and was connected with the lumbar subarachnoid space through the intervertebral foramen.

Examination of the brain and spinal cord showed that the ventricles were slightly enlarged. The leptomeninges covering the pons, optic chiasm, hypothalamus, hemispheral surfaces, and intrahemispheral fissures were greatly thickened and opaque.

The right thalamus was enlarged by a tumor, which had thickened the septum pellucidum and had involved the pituitary stalk and spread to the leptomeninges. The diffuse infiltrative process in the leptomeninges extended to the spinal cord, and the cauda equina was so thickened and infiltrated that there was little room for cerebrospinal fluid. The end of the polyethylene tube in the lumbar subarachnoid space was found to be free and patent, and it lay among the diffusely thickened, infiltrated nerve roots.

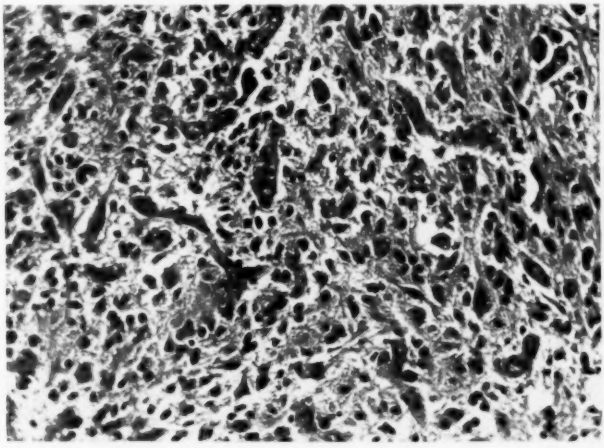

Fig. 1 (Case 1).—Astrocytoma, Grade 2, showing variation in size of cells and nuclei. Some giant nuclei are seen. There is increase in the number of small blood vessels but no increase in the cells of the intima or adventitia. There are no areas of necrosis. Mitotic figures are not seen here, and there were very few in the tumor. Hematoxylin-eosin stain; × 190.

On microscopic examination of sections stained in the routine manner, as well as with special methods, the tumor in the thalamus and its extension into the meninges proved to be an astrocytoma. The tumor was cellular, and there was some pleomorphism of the nuclei, together with some giant nuclei and an occasional giant cell. The walls of the blood vessels were not thickened; there were no areas of necrosis and but few mitotic figures. On the basis of this cytologic appearance, we considered this tumor to be an astrocytoma, Grade 2 (Fig. 1). Spicules of calcium were scattered throughout the tumor, but in insufficient amounts to be visible on roentgenographic examination of the head.

Necropsy demonstrated that the drainage of the subarachnoid spaces was entirely adequate. The polyethylene tube was patent. The presence of the tube in the spinal canal or in the peritoneal cavity did not appear to stimulate tissue reaction. The walls of the tube were thick enough to prevent kinking.

The true cause of the development of a communicating hydrocephalus was not suspected or revealed until necropsy. The clinical history revealed the temporary effects of medical regimens, drainage of cerebrospinal fluid, and ventriculomastoidostomy in the attempt to control communicating hydrocephalus. An exudative meningitis might well have closed the end of the tube, which was placed within the spinal canal. The drainage of cerebrospinal fluid may have been excessive in this case, and perhaps a tube of smaller caliber would have been sufficient. The technique we used provided enough drainage of cerebrospinal fluid to relieve the communicating hydrocephalus. The fluid was absorbed in the peritoneal cavity without giving rise to any untoward results.

Case 2.—A white boy aged 4 years was first seen at the clinic April 5, 1950, because of headaches and vomiting. One month earlier the child began to complain of headaches. These occurred almost daily and were severer in the left frontal region. Administration of acetylsalicylic acid was the only treatment that afforded any degree of relief. Occasionally, in association with the headaches, the patient complained of aching pains in the back of the legs, mostly on the left. The headaches and vomiting increased in severity, so that little food was retained. Just prior to admission to the clinic the parents had noted that the boy had a tendency to stagger.

General examination revealed a thin, pale, somewhat irritable child, who lay quietly in bed. Physical examination revealed nothing remarkable except for a soft, blowing systolic murmur over the precordium. Neurologic examination disclosed cracked-pot resonance of the skull and a staggering gait with tendency to veer to the left. There was some incoordination of the arms, more pronounced on the left. Reflexes were normal, and the Babinski sign was not elicited. Funduscopic examination showed bilateral papilledema of the subacute type, the degree of which was 4 D. on the left and 3 D. on the right. Vision seemed intact, and no nystagmus or change in the visual fields was elicited.

Electroencephalographic studies revealed the presence of right occipital delta waves, Grade 2, with generalized dysrhythmia, Grade 1. During hyperventilation there was a generalized increase in activity. Laboratory studies all gave normal results. Roentgenograms of the skull revealed the pituitary fossa to be slightly enlarged, and there was some decalcification of the dorsum sellae turcicae. There was also widening of the cranial sutures.

On April 8, bilateral suboccipital craniectomy was performed. When the dura was opened, the arachnoid was found to be densely adherent to the brain and greatly thickened. The posterior cistern was dilated, and the fourth ventricle measured about 2 cm. in diameter. The inferior end of the aqueduct was readily visible.

The diagnosis of communicating hydrocephalus secondary to chronic adhesive arachnoiditis was made. Pieces of arachnoidal tissue were taken to be studied for the presence of tuberculosis, but subsequent reports failed to confirm this possibility.

After operation, there was bulging at the site of the suboccipital decompression, and a fistula developed from which drained cerebrospinal fluid. Subsequently, it became necessary to insert a ureteral catheter into the lumbar subarachnoid space to afford drainage. This catheter allowed drainage of from 60 to 120 cc. of cerebrospinal fluid in a period of six to eight hours. A more permanent type of drainage of the subarachnoid space became necessary. Consequently, ventriculomastoidostomy, with a technique similar to that described by Nosik,[8] was performed on the right side. After this procedure the tissues overlying the site of the suboccipital decompression became soft. The patient looked well, appeared cheerful, and ate his meals in a satisfactory manner; but in a short time the site of the decompression became tense again. The temperature became elevated to 102 F.; the patient ceased to respond to verbal command and lapsed into rigidity of the hyperextensor type. Temporary relief was obtained by drainage of the cerebrospinal fluid which had collected between the cerebellum and the cervico-occipital muscles.

On the 12th postoperative day the site of the ventriculomastoidostomy was examined to determine the patency of the polyethylene tube. No obstruction was found. Biopsy of the arachnoid disclosed the presence of a chronic proliferative process.

Since the child continued to remain very ill and to display evidence of greatly increased intracranial pressure, a second ventriculomastoidostomy was performed on the left side, on April 19. From this ventriculomastoidostomy opening sufficient cerebrospinal fluid could not be drained to provide relief of the symptoms. A silk seton was introduced into the spinal canal, with equally poor results. Actual drainage of cerebrospinal fluid with a needle was necessary to prevent opisthotonos.

In the hope that irradiation of the head might decrease the secretion of cerebrospinal fluid, a course of 1,600 mg.-hr. of radium irradiation was administered. On June 10, 11 days after radium therapy was started, the child's condition was improved. The site of the suboccipital

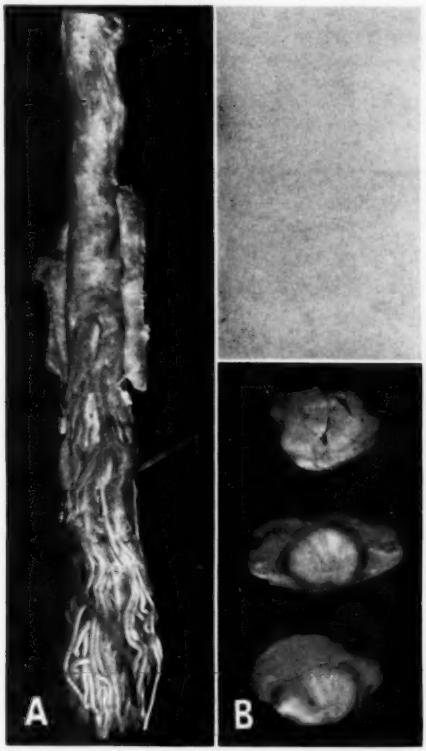

Fig. 2 (Case 2).—*A*, lower portion of the spinal cord and cauda equina. The polyethylene tube is seen in the subarachnoid space among the nerve roots. Note that the spinal cord and upper portion of the cauda equina are encased in a mass of tumor. *B*, cross sections of three levels of the spinal cord, which is surrounded, and in places invaded, by the tumor.

decompression became soft and was reduced in size. The patient was mentally clearer, was able to eat, and appeared to feel much better. He was actually able to be up and about for a few minutes and was therefore dismissed from the hospital. One week later he was readmitted to the hospital because the site of the suboccipital decompression was again bulging, and because repeated spinal or suboccipital aspirations of cerebrospinal fluid had become necessary. In July symptoms and signs of acute purulent meningitis appeared, and cultures of the cerebrospinal fluid revealed the presence of Escherichia coli and Streptococcus fæcalis. The meningitis was controlled with antibiotics, and on Aug. 19 cultures of the cerebrospinal fluid were sterile.

Since cerebrospinal fluid continued to collect under the flap in the suboccipital area, we thought it worth while to attempt drainage of the cerebrospinal fluid into the peritoneal cavity by means of a polyethylene tube. The operation was carried out on Sept. 16, 1950.

For a time after operation the patient appeared to improve, but gradually his condition became worse, and, despite all efforts and supportive therapy, he died, on Nov. 4, 1950.

Necropsy revealed marked emaciation. Gross examination revealed essentially nothing abnormal. Both lungs contained many mucous plugs in the bronchioles, and there was pulmonary edema.

The peritoneal surface was smooth and glistening, and there were no tumor implants. A polyethylene tube was seen to extend for a distance of about 2 cm. into the peritoneal cavity at the level of the 12th rib just above the lower edge of the liver. The tube was patent at this location. No peritoneal reaction to the presence of the tube was noted.

A large suboccipital meningocele, measuring approximately 7 by 6 by 5 cm., was found. The brain was under much pressure, as evidenced by flattening of the convolutions. Hydrocephalus was noted, and all the ventricles were greatly distended. A tumor mass was present over the left cerebral hemisphere. This tumor had spread so that it involved the meninges

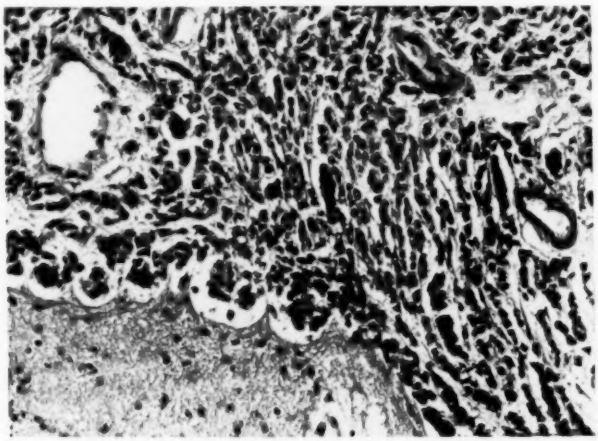

Fig. 3 (Case 2).—Typical meningothelial type of meningeal meningiomatosis. Hematoxylin-eosin stain; × 170.

diffusely. The same grayish tumorous infiltration was present over the base of the brain, ensheathing the medulla oblongata and involving the spinal cord inferiorly as far as the cauda equina.

The cauda equina was embedded in the grayish, diffuse, thick, plastic infiltrating tumor. The polyethylene tube was seen to lie among these rootlets (Fig. 2*A*), and the mouth of the tube had become completely occluded by tumor growth.

When the degree of involvement of the entire brain and spinal cord (Fig. 2*B*) by tumor growth was seen, it was obvious why little relief of the hydrocephalus was obtained.

Microscopically the neoplastic process was a primary diffuse tumor of the meninges. This tumor was typical of the group which we have designated as meningothelial type of diffuse tumor of the meninges (Fig. 3). It was made up of meningothelial cells, which in some places had produced a pronounced fibroblastic reaction in the meninges. In spite of its apparent high degree of malignancy, there was little pleomorphism and few mitotic figures.

We have seen a number of such tumors in the past; they occur most commonly in young persons, but not as a rule in infants. In this tumor, as in other primary

diffuse tumors of the meninges, there was no large mass or focus from which spread throughout the meninges could arise. Therefore we consider that the meningothelial type of tumor may have a diffuse origin.

OPERATIVE TECHNIQUE

In the past, when attempts have been made to drain cerebrospinal fluid into the peritoneal cavity the communicating channel or tube has become occluded. It occurred to one of us (Adson) that if a thick plastic tube could be carried from the lumbar portion of the canal into the peritoneal cavity over the liver it might be possible to effect drainage of cerebrospinal fluid into the peritoneal cavity.[11]

The following surgical procedure is employed to accomplish this drainage. The patient is placed on his left side, so that two incisions can be made. One

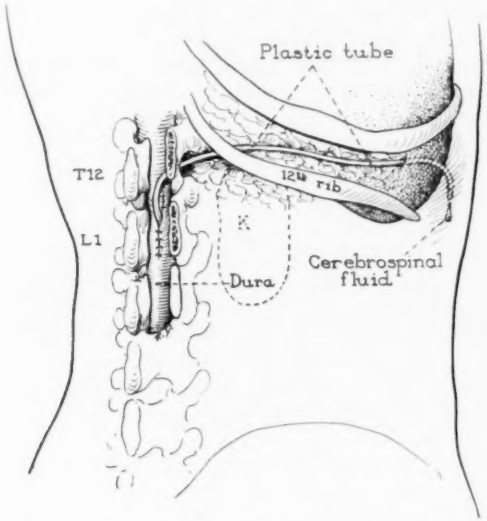

Fig. 4.—Position of the polyethylene tube which carries cerebrospinal fluid from the spinal canal into the peritoneal cavity.

incision is made for the thoracolumbar laminectomy, and the other is made parallel with the 12th rib through Petit's triangle in order to direct the plastic tube above the kidney and into the peritoneal cavity over the lower edge of the liver. After laminectomy a small opening is made in the dura and arachnoid in order that the plastic tube may be inserted downward for a distance of 4 cm. into the lumbar portion of the canal. The openings are closed with silk suture. The loose ends of the suture are then wrapped around the tube and tied to prevent slipping of the tube. After the roots of the 12th thoracic nerve on the right side are sectioned, the free end of the tube is directed through the intervertebral foramen into the

11. Ferguson, A. H.: Intraperitoneal Diversion of the Cerebrospinal Fluid in Cases of Hydrocephalus, New York M. J. **1**:902 (June) 1898.

perirenal space. A dissection then is made between the peritoneum lying over the liver and the abdominal wall to the level of the inframammary line. At this point a small opening is made in the peritoneum. The tube is now placed loosely in the perirenal space, so that there is no danger of the tube being withdrawn from either the spinal canal or the peritoneal cavity when the patient moves. The tube is inserted into the peritoneal cavity and extended for a distance of 2 cm. below the margin of the liver (Fig. 4).

SUMMARY

Reports of two cases are presented in which communicating hydrocephalus was a result of diffuse involvement of the meninges by tumor.

A surgical technique is described whereby a polyethylene tube is placed between the subarachnoid space and the peritoneal cavity in an attempt to drain excessive amounts of cerebrospinal fluid and thus relieve the increased intracranial pressure.

Our reason for reporting these two cases is not to advocate an operative procedure for communicating hydrocephalus when this is the result of spread of a neoplasm diffusely through the meninges, but, rather, to emphasize that such drainage may be of value in the management of chronic communicating hydrocephalus after the acute stage of leptomeningitis has subsided.

VASCULAR MALFORMATIONS OF THE SPINAL CORD

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A REVIEW of 31 cases with necropsy which presented a clinical picture of transverse or diffuse "myelitis" revealed the striking fact that in 9 the lesion of the cord was a myelomalacia secondary to malformation of the vessels of the spinal cord. These nine cases, in five of which the lesions were diffuse and in four focal, are considered in the present report.

Knowledge of such malformations is not new. The presence of vascular abnormalities has been noted by neurosurgeons in certain cases of spinal compression. Numerous reports of this association have appeared in the literature.[1] Congenital malformations may also result in a myelitic picture of a special type, and this was first described by Foix and Alajouanine [2] as *myélite nécrotique subaigue.*

The clinical characteristics given by these authors were of progressive paraplegia, at first spastic, then flaccid with atrophy, the process advancing slowly upward in the spinal cord. A short time later, dissociated sensory disturbances appeared, with sparing of touch sense at first but with the dissociation becoming total afterward and progressing upward. The cerebrospinal fluid contained a large amount of protein, with albuminocytologic dissociation. Death occurred in one to three years.

Anatomic findings included a predominantly central necrosis of the lower part of the spinal cord, pure at lumbosacral levels, mixed with hemorrhages in the lower dorsal level, and ending in the midthoracic region. Associated with this necrosis, an intense *endo-meso-vascularite* was encountered, as well as an increased number of leptomeningeal vessels, which were enlarged, and were thick in the lumbar region but thinner above. The intramedullary vessels were also altered, being more

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Boursier de la Direction Générale des Rélations Culturelles du Ministère des Affaires Etrangères de France (Dr. Brion).

1. (*a*) Sargent, P.: Hemangioma of the Pia-Mater Causing Compression Paraplegia, Brain **48**:259-267, 1925. (*b*) Raymond, E., and Cestan, R.: Un cas d'anévrisme cirsoïde probable de la moëlle cervicale, Rev. neurol. **12**:457-463, 1904. (*c*) Globus, J. H., and Doshay, L. J.: Venous Dilatations and Other Intraspinal Vessel Alterations, Including True Angiomata, with Signs and Symptoms of Cord Compression, Surg., Gynec. & Obst. **48**:345-366, 1929.

2. Foix, C., and Alajouanine, T.: La myélite nécrotique subaiguë. Myélite centrale angéiohypertrophique à évolution progressive, paraplégie amyotrophique lentenment ascendante, d'abord spasmodique, puis flasque, s'accompagnant de dissociation albumino-cytologique, Rev. neurol. **2**:1-42, 1926.

numerous than usual, and hyalinized. The authors thought the alteration of vessels was responsible for necrosis of the cord but insisted that they had not found thrombi or occlusions.

During the following years, similar pictures were reported by others.[3] In contrast, in other cases of a condition called subacute necrotic myelitis or myelopathy the picture seems to be completely different anatomically but for the necrosis.[4] A general review of vascular malformations of the spinal cord was presented by Wyburn-Mason[5] in 1943. More recently, subacute necrotic myelitis has been considered by Stolze.[6]

REPORT OF CASES

A. Diffuse Malformations.—CASE 1.—I. M., a white man aged 48, had a history of cramps starting in 1928 and involving both calves after walking. A diagnosis of thromboangiitis obliterans (Buerger's disease) was made at this time. In 1936 he noted the progressive onset of numbness and tingling in both legs and of ataxia when walking. In 1938 his legs became progressively weaker, and by November, 1939, he was bedridden. He was admitted to another hospital in December, where a myelogram was reported as normal. Transfer to the Montefiore Hospital was made in February, 1940, where flaccid paraplegia and atrophy of the proximal muscles of both lower extremities were found. The deep reflexes, the cutaneous abdominal reflexes, and the Babinski sign were all absent. Anesthesia for all modalities was complete up to the 12th thoracic dermatome, with hypesthesia from the 1st to the 12th thoracic. There was incontinence of urine. The upper limbs were not involved, and the cranial nerves were intact. Examination of the cerebrospinal fluid revealed 2 lymphocytes per cubic millimeter, 74 mg. of protein per 100 cc., a negative Wassermann reaction, and a normal colloidal gold curve. Manometric studies of the spinal fluid gave normal results. The only abnormality in the blood count was eosinophilia, the count being as high as 17%.

The condition of the patient remained almost the same, with only slight improvement after x-ray treatment. During the following years the sensory level ascended to the 10th thoracic dermatome for complete anesthesia and the 5th thoracic dermatome for hypesthesia, and bedsores developed.

In 1945 a hypernephroma of the left kidney was discovered, for which nephrectomy was performed. The patient died shortly after this procedure, nine years after appearance of the first neurologic sign. The clinical diagnosis was myeloradiculopathy.

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3. (*a*) Lhermitte, J.; Fribourg-Blanc, A., and Kyriaco, N.: La gliose angéio-hypertrophique de la moelle épinière (Myélite nécrotique de Foix-Alajouanine), Rev. neurol. **2**:37-53, 1931. (*b*) Greenfield, J. G., and Turner, J. W. A.: Acute and Subacute Necrotic Myelitis, Brain **62**:227-252, 1939. (*c*) Minea, I.: Cited by Greenfield and Turner.[3b] (*d*) Marinesco, G., and Draganesco, S.: Formations télangiectasiques méningées avec processus angiomateux intramedullaires, Rev. neurol. **63**:809-827, 1935.

4. van Gehuchten, P.: Un cas de myélite nécrotique aiguë, Rev. neurol. **1**:505-519, 1927. van Bogaert, L.; Ley, R. A., and Brandes, F.: Contribution anatomo-clinique à l'étude de la myélite nécrotique subaiguë de Foix-Alajouanine, ibid. **2**:1-27, 1930. Marinesco, G., and Draganesco, S.: Myélite nécrotique aiguë, Ann. med. **31**:5-20, 1932. Riser, G., and Planques, A.: De l'encéphalomyélite nécrotique subaiguë, Rev. neurol. **67**:455-476, 1937. Juba, A.: Myelitis Necroticans Subacuta (Foix-Alajouanine), Deutsche Ztschr. Nervenh. **148**:17-30, 1938. Dansmann, W.: Über die sog. Myelitis necroticans subacuta, Ztschr. ges. Neurol. u. Psychiat. **168**:644-659, 1940. Davison, C., and Brock, S.: Subacute Necrotic Myelopathy: A Fatal Myelopathy of Unknown Origin, J. Neuropath. & Exper. Neurol. **3**:271-288, 1944. Juba, A.: Über die myelitis necroticans subacute, Monatsschr. Psychiat. u. Neurol. **114**:225-235, 1947.

5. Wyburn-Mason, R.: The Vascular Abnormalities and Tumors of the Spinal Cord and Its Membranes, London, Henry Kimpton, 1943.

6. Stolze, H.: Anlageanomalien der Rückenmarksvenen und Foix-Alajouaninesches Syndrom, Arch. Psychiat. **185**:370-394, 1950.

Necropsy revealed evidence of the left nephrectomy, with local recurrence and widespread metastases of carcinoma of the kidney, and pyelonephritis in the remaining kidney.

Macroscopic examination of the nervous system failed to reveal abnormalities in the brain. In the leptomeninges on the posterior surface of the spinal cord were numerous tortuous vessels, extending from the midthoracic to the lumbar region (Fig. 1). These vessels compressed the

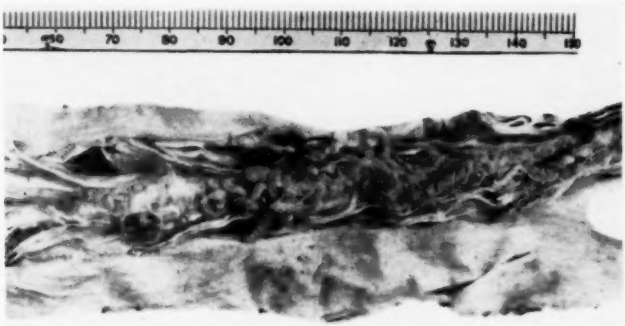

Fig. 1 (Case 1).—The tangle of malformed vessels on the posterior surface of the spinal cord is shown in this photograph. The lower part of the cord is on the right. The scale is in millimeters.

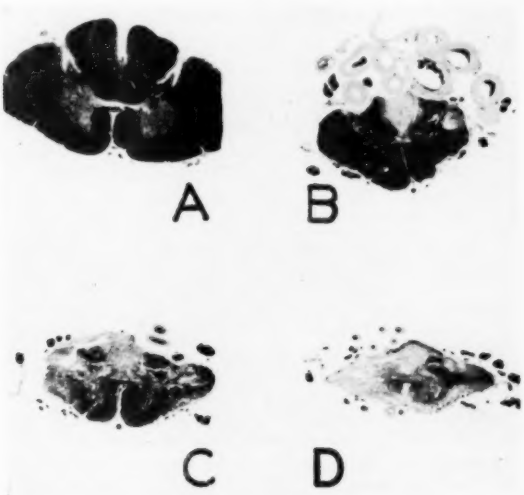

Fig. 2 (Case 1).—(*A*) There is ascending demyelination in the cervical region of the spinal cord. (*B*) A cluster of large arteries is present on the posterior surface of the middle part of the thoracic spinal cord. There is both ascending and descending demyelination. (*C*) At low thoracic levels the demyelination is more diffuse. (*D*) The shrunken lumbar portion of the cord is extensively demyelinated. The abnormal arteries are almost completely occluded and are predominantly in the posterior portion. × 3; Weil stain.

posterior columns, flattening the posterior and lateral parts of the lumbar and sacral regions of the cord. The posterior columns above the mass of vessels had a chalky appearance.

Microscopic examination revealed that the posterior surface of the cord from the lumbar to the high thoracic level was covered and compressed by a tangle of large arteries, numbering 10 to 12 and situated in the leptomeninges (Fig. 2). Most of the vessels were rather large and had greatly thickened walls. The media had proliferated and formed successive layers, separated by concentric zones of hyalin (Fig. 3*A*). The elastica, though frayed, was well seen (Fig. 3*B*). The subendothelium was thick and contained atherosclerotic plaques. The adventitia was normal. In addition, the lumens of many vessels were obliterated by thrombi in various stages of organization. Between these arteries a few dilated, but otherwise normal, veins were seen.

On the anterior surface of the cord there were two malformed arteries, which lay on either side of the normal anterior spinal artery (Fig. 3*A*). The abnormal vessels were more numerous in the midthoracic than in the lumbar region. At the lumbar level, however, most of the vessels were thrombosed and shrunken.

Within the spinal cord there were complete demyelination and old necrosis at lumbar levels. In the thoracic region there was complete demyelination in the fasciculus gracilis, but patches of demyelination and old necrosis were present in the lateral tracts. At cervical levels only demyelination of the fasciculus gracilis was observed. The neurons were fairly well preserved except in the necrotic lumbar and low-thoracic levels. The vessels within the cord were altered up to a high-thoracic level. They were increased in number, especially in the posterior half of the cord, and frequently were arranged in clusters of three or four. These vascular changes were seen in uninvolved parts of the spinal cord, as well as in demyelinated areas.

Comment: The clinical picture of progressive flaccid paraplegia indicated a process causing severe destruction of the lower part of the cord. This process slowly ascended, as shown by the rise of the sensory level. The intermittent cramps were not due to thromboangiitis obliterans, but probably were secondary to minimal root compression. The anatomic findings well explain the clinical picture. There was an arterial malformation involving the lower half of the spinal cord. The lesions of the cord were secondary in part to the ischemia of vascular thrombosis and in part to compression of the posterolateral part of the cord by the enlarged vessels.

Case 2.[7]—H. B., a white man aged 40, had been well until March, 1941, when intermittent pains suddenly were felt in the sole of the left foot. One month later he noted progressive weakness of both legs. In the middle of May there were severe shooting pains in the feet, legs, and thighs. These pains came on while he was walking and disappeared during rest. The diagnosis of thromboangiitis obliterans was made. At about this time urinary retention began. The patient was admitted to another hospital at the end of May, 1941. Incomplete flaccid paraplegia and a sensory level at the first lumbar dermatome were found. The cerebrospinal fluid contained 5 cells per cubic millimeter and 59 mg. of protein per 100 cc. A myelogram showed only a slight delay in dye movement, at the lower border of the fourth lumbar vertebra. Laminectomy, in June, 1941, revealed abnormal vessels on the left side of the lumbar portion of the cord, conus, and filum terminale, as well as among the roots on the right side. These vessels were pulsating and filled with bright red blood. The patient was transferred to the Montefiore Hospital in July, 1941, with the diagnosis of arterial malformation of the spinal cord. Examination revealed complete flaccid paraplegia with mild diffuse atrophy and absence of deep reflexes in the lower extremities. The Babinski sign was absent, as were the cutaneous abdominal reflexes. There was complete superficial anesthesia from the 10th thoracic dermatome down and hypesthesia from the 7th to the 10th thoracic dermatome. The upper limbs and the cranial nerves were intact.

Pains in the thighs and legs persisted. An ascending urinary-tract infection necessitated, first, a suprapubic cystostomy and, later, right orchidectomy for testicular abscess. The neurologic condition of the patient remained unchanged until his death, in December, 1947, six years

7. This case has been reported previously (Epstein, J. A.; Beller, A. J., and Cohen, I.: Arterial Anomalies of the Spinal Cord, J. Neurosurg. **6**:45-56, 1949).

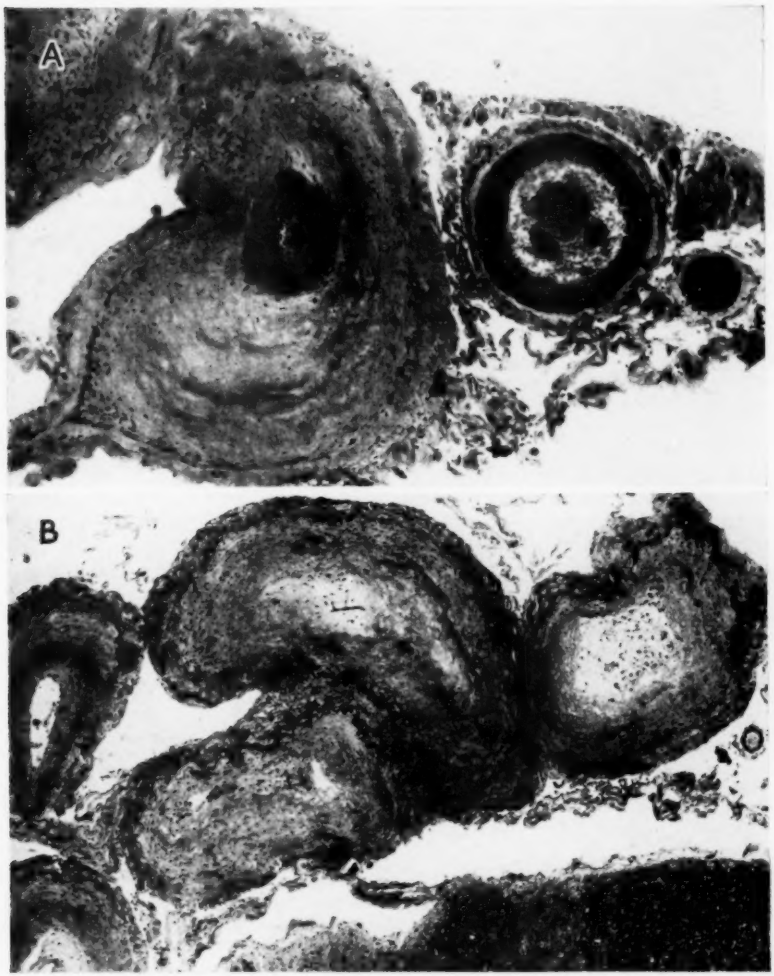

Fig. 3 (Case 1).—(*A*) On the anterior surface of the thoracic portion of the spinal cord, two malformed vessels surround the normal anterior spinal artery. The artery to the left has undergone extensive medial thickening. The small vessel on the right side is occluded by endothelial proliferation. × 120; hematoxylin-eosin stain.

(*B*) The arteries on the posterior surface are occluded by old organized thrombi. The frayed elastica can be seen. × 48; hematoxylin-eosin stain.

after onset of the illness. The clinical diagnosis was arterial malformation of the spinal cord with flaccid paraplegia.

Necropsy revealed bilateral pyoureter, pyonephrosis, and pyelonephritis.

Only the thoracic and lumbar portions of the spinal cord were removed. A postoperative dural scar with adhesions was observed on the posterior aspect of the cord at the level of the conus. At the uppermost level of the operative incision there was a small vascular anomaly in the leptomeninges, consisting of a few collapsed blood vessels. Arachnoidal adhesions bound the cord and the cauda equina. The thoracic region of the spinal cord and the nerves of the cauda equina were atrophic. There was loss of demarcation between gray and white matter in the thoracic region, and the white matter in the lumbosacral enlargement was gray.

Histologic examination revealed large abnormal vessels around the lumbar portion of the cord, mostly on one side. They consisted of large channels, having thick, collagenous walls (Fig. 4*A*). The lumens usually were irregularly enlarged. The endothelial lining was often absent, and there were old concentric thrombi, with complete occlusion of one of the large vessels. Smaller vessels with similar changes were encountered in the meninges in the anterior sulcus and also in the anterior roots. All the involved vessels were venous in type. The arteries were normal. At thoracic levels there were similar changes, but less prominent.

Within the cord there was demyelination at the lumbar level, with intense replacement gliosis. In addition, there was old necrosis of the posterior half of the cord. Similar lesions were seen at the thoracic level, but part of the anterior horns and the adjacent white matter were spared. Many anterior horn cells had disappeared; the remainder were altered, many with axonal change. The roots of the cauda equina were partially demyelinated.

Within every part of the cord, whether altered or not, the veins were increased in number and arranged in clusters. They had thick hyaline walls (Fig. 4*B*). Many were occluded by thickening or old thrombi. The arteries in the cord were only slightly thickened.

Comment: The clinical picture indicated a slow, severe destruction of the lower part of the cord. The onset was with pain in the left foot, and in this case, as in Case 1, an erroneous diagnosis of thromboangiitis obliterans was made. The process remained localized to the lower half of the cord.

The major lesion was a vascular malformation, purely venous in type. It is interesting that when the lesion was exposed at laminectomy the channels were noted to be filled with bright red blood and, for this reason, were interpreted as arteries.[7] The spinal cord was not compressed. The parenchymatous lesions were most intense posteriorly, where the majority of malformed veins was present.

Case 3.—D. R., a Negro aged 39, had onset of progressive weakness of both legs in 1930. At this time the Wassermann reaction of the blood was negative, although there was a history of a penile chancre in 1925 and of a cutaneous ulcer of the left leg in 1929. The patient was treated irregularly for syphilis with arsenic and bismuth until 1936. The weakness, however, increased slowly. In 1933 the Wassermann reactions of both blood and cerebrospinal fluid were negative. In 1934 the blood gave a positive reaction once after a provocative test, but never the cerebrospinal fluid. In 1936 the patient received malarial therapy, and complete paraplegia with urinary incontinence developed rapidly thereafter. In 1938 the Wassermann reaction of the blood was positive.

On his admission to the Montefiore Hospital, in March, 1942, examination revealed flaccid paraplegia, more intense on the left side, with some wasting and fasciculations. The upper limbs were not involved. The cutaneous abdominal reflexes were absent, as were the deep reflexes in the lower extremities. A Babinski sign was not elicited. There was complete anesthesia up to the fourth lumbar level bilaterally. Facial paralysis of supranuclear type was present on the left, and there were congenital cysts in both retinas. The Wassermann reaction of the blood was negative. The cerebrospinal fluid contained 2 white blood cells and 23 red blood cells per cubic millimeter, and 48 mg. of protein per 100 cc.; the Wassermann reaction was negative, and the gum mastic curve was normal.

The neurologic picture remained unchanged. During his hospitalization there developed cardiac hypertrophy, hypertension, and diffuse arteriosclerosis. At the end of May, 1942, he

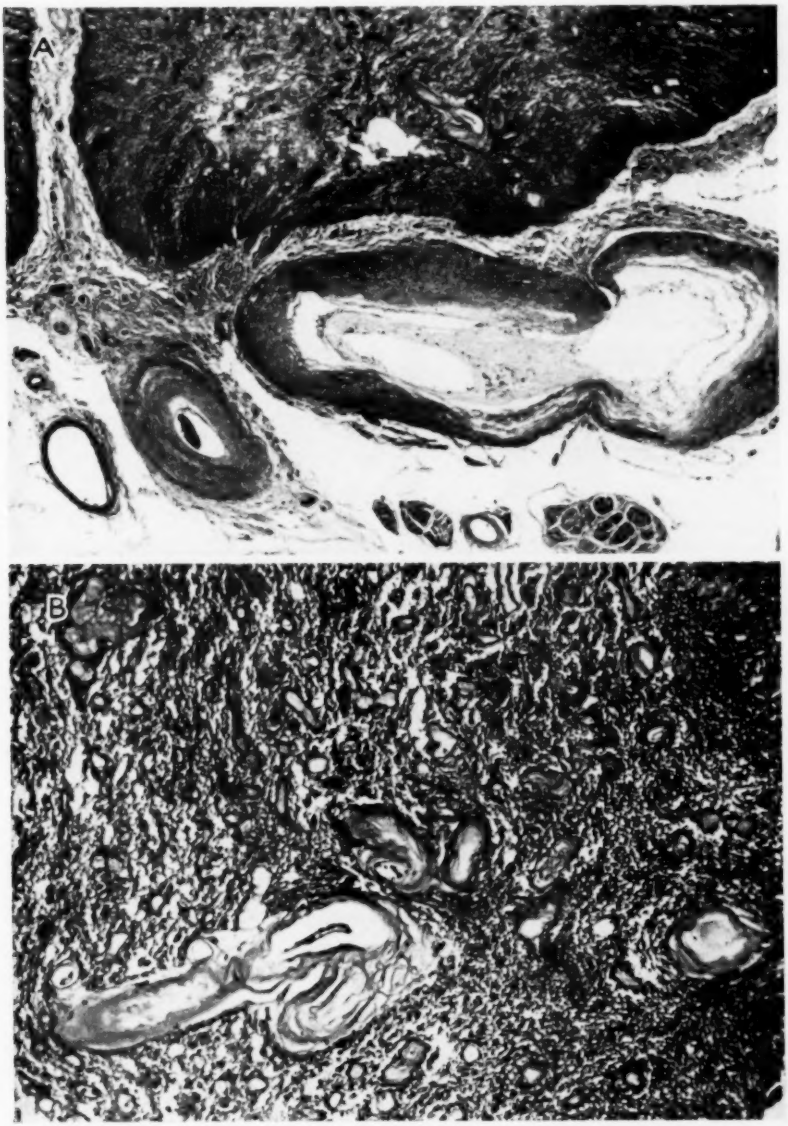

Fig. 4 (Case 2).—(*A*) This photomicrograph was taken near the anterior sulcus at the lumbar level. Two large, thick, malformed veins lie to the right of the normal anterior spinal artery. Similar small veins can be seen within the spinal cord. × 35; hematoxylin-eosin stain. (*B*) Intraspinal clusters of heavily fibrotic veins are seen in the lumbar region. × 120; hematoxylin-eosin stain.

suddenly complained of severe headache, lapsed into coma, and died shortly therafter, 12 years after the onset of the first neurologic symptom and 6 years after the onset of complete paraplegia. The clinical diagnosis was syphilis of the central nervous system.

Necropsy revealed an anomaly of the aortic valve, which was bicuspid, thick, and distorted. There was, in addition, atherosclerosis of the aorta, but no scars or evidence of mesaortitis. The left ventricle was hypertrophied, and there was bilateral chronic pyelonephritis. A diffuse subarachnoid hemorrhage was present at the base of the brain and spinal cord, extending down to the lower part of the spinal cord. A ruptured aneurysm of the right posterior communicating artery was found. In the lower part of the spinal cord were many congested, tortuous vessels. The posterior columns appeared demyelinated.

Histologic examination revealed numerous large veins and arteries surrounding the cord from the low thoracic to the sacral level, mostly on the posterolateral surface (Fig. 5). The veins had elongated lumens and thick, fibrous walls, which contained concentrically arranged, but interrupted, elastic fibers. The endothelium was absent in places, and there were organized

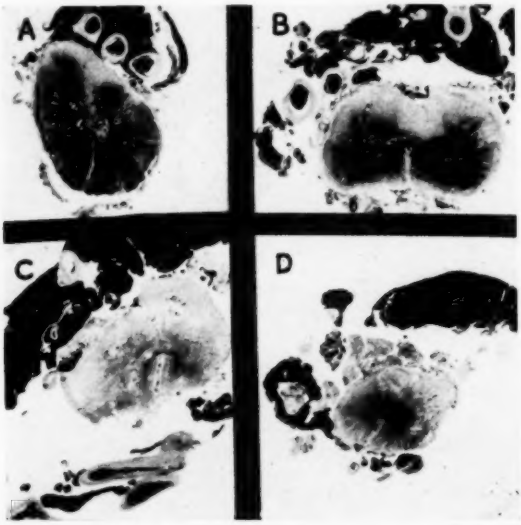

Fig. 5 (Case 3).—(*A*) In the thoracic region, large veins and arteries are seen on the posterior surface. There are ascending demyelination and patchy demyelination elsewhere. The dark mass is fresh blood in the subarachnoid space, secondary to rupture of a cerebral aneurysm. (*B*) There is a similar alteration in the upper lumbar region. (*C*) The spinal cord is necrotic in the lower lumbar portion. Intramedullary malformed vessels can be seen. (*D*) The sacral part of the spinal cord is similarly altered. × 4; Weil stain.

thrombi. The arteries also were voluminous, and their lumens were reduced in size as a result of enormously thick walls. This thickening was due to proliferation of both the media and the subendothelial connective tissue. The arteries contained atheromatous patches, a disrupted tunica elastica, and irregular calcifications of the media. Similar, but smaller, abnormal vessels were seen in the roots.

The intraspinal vessels were more numerous than usual. This increase was diffuse at thoracic, lumbar, and sacral levels, but were always more prominent in the posterior half of the cord. The vessels were sometimes isolated, but were oftener arranged in clusters or rows. The veins and arteries were not only thick but occasionally occluded. The spinal parenchyma was almost completely destroyed. At lumbosacral levels the cord was softened and its posterior half replaced by intense gliosis, with more recent necrosis anteriorly. In the low-thoracic region there was

complete demyelination of the posterior half of the cord, with glial proliferation, but necrosis was absent.

At the level of the medulla, numerous enlarged arteries were present along the anterior surface.

Comment: Clinically, the evidence in this case was misleading because of an old history of syphilis. There was never any support, however, for a syphilitic origin of the paraplegia; the cerebrospinal fluid at all times was serologically negative. There were no data on the character of the paraplegia in the first six years, but later it was flaccid and remained so. The course was chronic, and the patient died with a subarachnoid hemorrhage from a ruptured aneurysm of the posterior communicating artery.

There were diffuse arterial and venous malformations in the lower part of the spinal cord, with destruction of the fiber tracts and neurons in the lumbar region. At the thoracic level, the changes consisted partly of an ascending demyelination and partly of necrosis due to the malformation. An interesting additional finding was the arterial malformation on the anterior surface of the medulla.

CASE 4.[8]—L. R., a white man aged 46, was thrown from a street car in April, 1925, and became paraplegic a few minutes later. He was admitted to another hospital, where his legs were found to be paralyzed, cold, and numb. He had difficulty in starting the urinary stream and had burning on micturition. A few days later, he noted progressive obstipation. His condition remained unchanged, and he was transferred to the Montefiore Hospital in October, 1926. There was a history of "poliomyelitis" at the age of 6 months, with residual atrophy of the left leg and an equinovarus position of the left foot. Examination revealed flaccid paraplegia with atrophy of the thighs, absence of ankle jerks, and greatly diminished knee jerks. The Babinski sign was not present. The cutaneous abdominal reflexes were normal. There was tenderness on pressure of the first and second lumbar spinous processes. Complete loss of superficial sensation was found up to the 4th lumbar level, partial loss from the 1st to the 4th lumbar level, and hyperesthesia at the 11th and 12th thoracic level. Deep sensibility was absent below the first lumbar dermatome. There was severe retention of both urine and feces. The upper limbs and cranial nerves were intact. There were no meningeal signs. Examination of the cerebrospinal fluid revealed 3 to 15 lymphocytes per cubic millimeter, a positive reaction for globulin, a negative Wassermann reaction, a gum mastic curve of 2211100000 on one occasion and a normal curve on another. A roentgenogram of the spine showed arthritic bridges in the dorsolumbar region. Myelography was not performed. The neurologic condition of the patient remained unchanged. A persistent urinary-tract infection developed, and he died in August, 1928, three years after the onset of his neurologic disease. The clinical diagnosis was "degenerative" disease of the spinal cord.

Necropsy revealed cystitis, bilateral pyelonephritis, old apical tuberculosis, and bronchopneumonia. Examination of the nervous system was limited to the thoracic and lumbosacral portions of the spinal cord. There were prominent, tortuous vessels in the leptomeninges. When the cord was sectioned, the left side was found to have a chalky appearance.

Microscopic examination revealed that the lumbar and sacral levels of the cord were surrounded by numerous abnormal veins and arteries, more prominent on the anterior surface. The walls of all the veins were thickened by concentric proliferation, and the lumens of some were greatly reduced in size (Fig. 6*A*). The arteries had a greatly thickened subendothelial layer, with a resultant reduction in the size of the lumens. The elastica and media were normal. Similar abnormal vessels were encountered between the roots. At the thoracic level abnormal vessels were present for the most part on the anterior surface of the cord and in the anterior sulcus. The lumbar and sacral levels of the cord contained small hemorrhagic zones and fresh

8. This case has been reported previously (Keschner, M., and Davison, C.: Myelitic and Myelopathic Lesions: III. Arteriosclerotic and Arteritic Myelopathy, Arch. Neurol. & Psychiat. **29**:702-725, 1933).

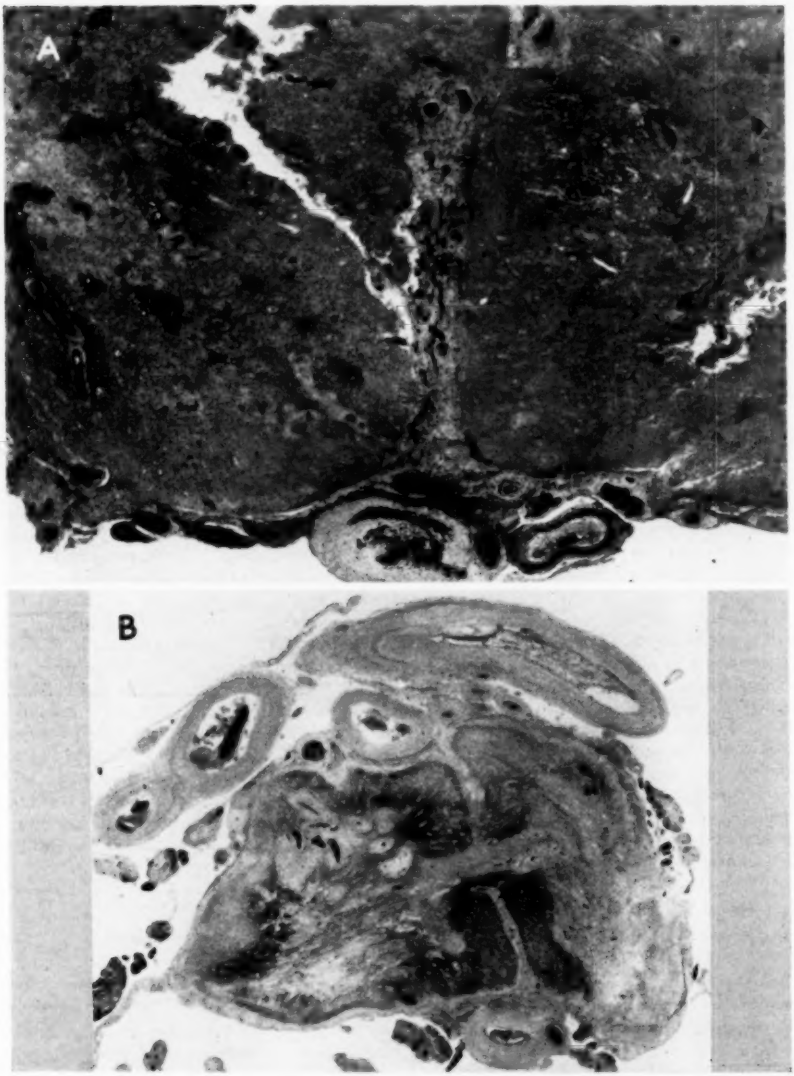

Fig. 6.—(*A*, Case 4) The necrotic spinal cord at the third lumbar level is seen in the upper part of the picture. Below, to the left, the anterior spinal vein is thick, and the reduced lumen contains a fresh thrombus. The wall contains a recent hemorrhage. The anterior spinal artery, on the right, reveals a subintimal proliferation. × 35; Weil stain.

(*B*, Case 5) There are numerous intramedullary and extramedullary veins and arteries at the lumbar level. The spinal cord is extensively softened and demyelinated. × 10; Weil stain.

and old areas of softening. Anterior horn cells were entirely lacking. Necrosis was complete at the sacral level and was most intense centrally in the lumbar region. A tremendous increase in the number of vessels was seen at these levels. They were frequently arranged in small clusters and were similar in appearance to those seen in the leptomeninges. The posterior columns and lateral tracts of the thoracic region were completely demyelinated.

Comment: The peculiarity of this case was the sudden onset of flaccid paraplegia immediately after trauma. Otherwise, it was similar to the preceding cases. The anatomic lesions consisted chiefly of arterial and venous malformations, both extramedullary and intramedullary, at lumbosacral levels, where the cord was destroyed by softening. At thoracic levels the lesions were mild. A question may be raised about the episode of so-called poliomyelitis, at the age of 6 months. This episode could have been either true poliomyelitis or the result of transitory damage to the cord secondary to the vascular malformation, but this question cannot be decided with certainty.

CASE 5.—H. L., a white man aged 46, at the end of 1942 noted progressive pain and weakness of the left leg and difficulty in walking. In March, 1943, he was admitted to another hospital, where a myelogram was reported as showing nothing abnormal except "a suspicious hang in flow" in the lower lumbar region. In July, 1943, the symptoms in the left leg increased, and the same difficulty was present on the right. In September, 1943, examination at still another hospital revealed "posterolateral-tract signs and a variable spinothalamic level." The deep reflexes in the lower extremities were increased. Lumbar puncture did not reveal block of the cerebrospinal fluid, but the protein content ranged from 128 to 224 mg. per 100 cc. and the cells from 5 to 10 per cubic millimeter. The myelogram was unsatisfactory, but suggested a lesion at the 10th thoracic vertebra. In December varicosities around the lower thoracic portion of the cord were seen at laminectomy. Subsequently, deep x-ray therapy was given. In April, 1944, just before his transfer to the Montefiore Hospital, there developed coldness of both legs, decubitus ulcers, and retention of urine.

Examination at this hospital revealed paraplegia with absence of the deep reflexes in the lower extremities and absence of the abdominal reflexes. The Babinski sign was not elicited. The muscles were flabby, although some observers described the paraplegia as spastic. There was a complete sensory level at the third thoracic dermatome. Examination of the cerebrospinal fluid revealed 4 white blood cells and 5 red blood cells per cubic millimeter and a protein content of 149 mg. per 100 cc. The Wassermann reaction was negative, and the mastic curve was normal, for both the spinal fluid and the blood.

The condition of the patient remained almost unchanged until shortly before his death, when further muscular atrophy was noted. He died of a urinary-tract infection and repeated attacks of bronchopneumonia, in December, 1945, after an illness of three years.

Necropsy revealed confluent bronchopneumonia, amyloidosis of the liver and spleen, chronic cystitis, and mild bilateral pyelonephritis.

The brain appeared normal on macroscopic examination. The leptomeninges of the spinal cord presented numerous varices from the 12th thoracic segment to the cauda equina. The cord was softened, and there was almost complete loss of the normal appearance in the low-thoracic and lumbar regions. Histologic examination revealed numerous thick and enlarged vessels surrounding the cord at the thoracic and lumbar levels (Fig. 6*B*). These predominated on the posterolateral surfaces of the cord and in the thoracic region. The vessels were both veins and arteries. The veins were enormously enlarged and had thick connective tissue walls. There was both medial and intimal proliferation of the arteries, while the adventitia was normal. The roots contained similar abnormal vessels.

Inside the lumbar region of the cord there was a significant increase in the number of vessels, which consisted for the most part of small veins with thick hyaline walls and almost occluded lumens (Fig. 6*B*). The arteries were less numerous, but were also thick and reduced in caliber. The vessels in the parenchyma were arranged in clusters of three to five. There was extensive necrosis of the cord with invasion by macrophages and astrocytes. Many cells in the anterior horns had disappeared or were altered. At the thoracic level, the intramedullary vascular

abnormalities were less conspicuous. The lesions were similar, but less intense, and there were only alteration of the anterior horn cells and patchy demyelination of the posterior half of the cord. At the cervical level ascending demyelination of the fasciculus gracilis was present.

Comment: This patient had severe paraplegia, which was described as spastic. However, in view of the flabbiness of the muscles, the absence of deep reflexes and of the Babinski sign, and the rapid progression of muscular atrophy, it is more likely that the paraplegia, which had been spastic in the beginning, later became flaccid with secondary contractures. This conclusion was confirmed by the extensive loss of anterior horn cells in the lower parts of the spinal cord. Histologic examination revealed an extensive arterial and venous malformation, both intramedullary and extramedullary, at the thoracic and lumbar levels. This secondarily gave rise to partial necrosis of the lumbar part of the cord, but to simple demyelination elsewhere.

B. Focal Malformations.—Case 6.[8]—E. G., a white woman aged 42, had onset of pain in the extensor surface of the right foot in October, 1917. This was paroxysmal and shock-like and occurred five to six times a day. It was accompanied or followed by spasms of the extremity, in which the leg would flex at the knee and the hip. This condition would last 15 minutes, but between attacks the gait was normal. Four months later the pain rose to the knee, to the hip, and to the kidney region, increasing in severity, frequency, and duration. The left leg was free from any symptom. Seven months after onset, in April, 1918, a laminectomy between the first and the fifth thoracic vertebrae—performed at another hospital—failed to disclose tumor, but the spinal cord was said to be atrophic. The symptoms in the right lower extremity persisted. In addition, the patient complained of rigidity of the abdominal muscles, of the sensation of a tight band over the lower part of the chest, and of urinary retention.

She was transferred to this hospital in June, 1918, presenting intense spastic paraplegia with flexion of both lower extremities, more pronounced on the right side. Cutaneous abdominal reflexes were absent. There was a Babinski sign bilaterally. Anesthesia was complete up to the fourth thoracic dermatome. Wasting of the supraspinatus, elevator anguli scapulae, and trapezius muscles was noted on the right side. There were diminution of motor power of the right upper limb and slight atrophy of the muscles of the right hand. There were no abnormalities in the cerebrospinal fluid. Routine examinations of the blood and urine were similarly unrevealing. In 1919 moderate spastic paralysis appeared in the right upper limb. In 1920 there were a band of hyperesthesia at the third cervical dermatome, hypesthesia between the third cervical and the fourth thoracic segment, and complete anesthesia below. Both upper limbs became spastic in 1922. In 1926 there was astereognosis in both upper limbs, in addition to the spasticity. During this time the paraplegia remained unchanged. Bronchopneumonia developed, and she died in February, 1930, 13 years after the appearance of the first neurologic sign.

Necropsy revealed generalized arteriosclerosis, ulceration and intramural thrombi in the abdominal aorta, chronic cystitis, and bronchopneumonia.

Examination of the brain revealed a small meningioma in the left temporal lobe and several areas of discoloration in the centrum ovale, around the lateral ventricle. The spinal cord, which was removed from the sixth thoracic segment to the sacral region, contained an area of softening at the thoracic level.

Histologic examination revealed an old softened zone with demyelination and replacement gliosis occupying the posterior part of the spinal cord between the sixth and the ninth thoracic segment (Fig. 7*A*). The cord was distorted at these levels and contained a large number of abnormal veins, with thick, reduplicated walls and extreme reduction of the lumens. These vessels were frequently arranged in clusters of three or four and were seen even in the nondemyelinated portions of the cord. Thrombosed vessels were not encountered. Several abnormal veins and a normal anterior spinal artery were seen within the leptomeninges. A few of these veins penetrated the posterior septum and were also present in the roots.

At the lumbar level, a few malformed veins were seen in the anterior sulcus, in the roots, and in small clusters in the anterior horns. There was also a descending demyelination; in

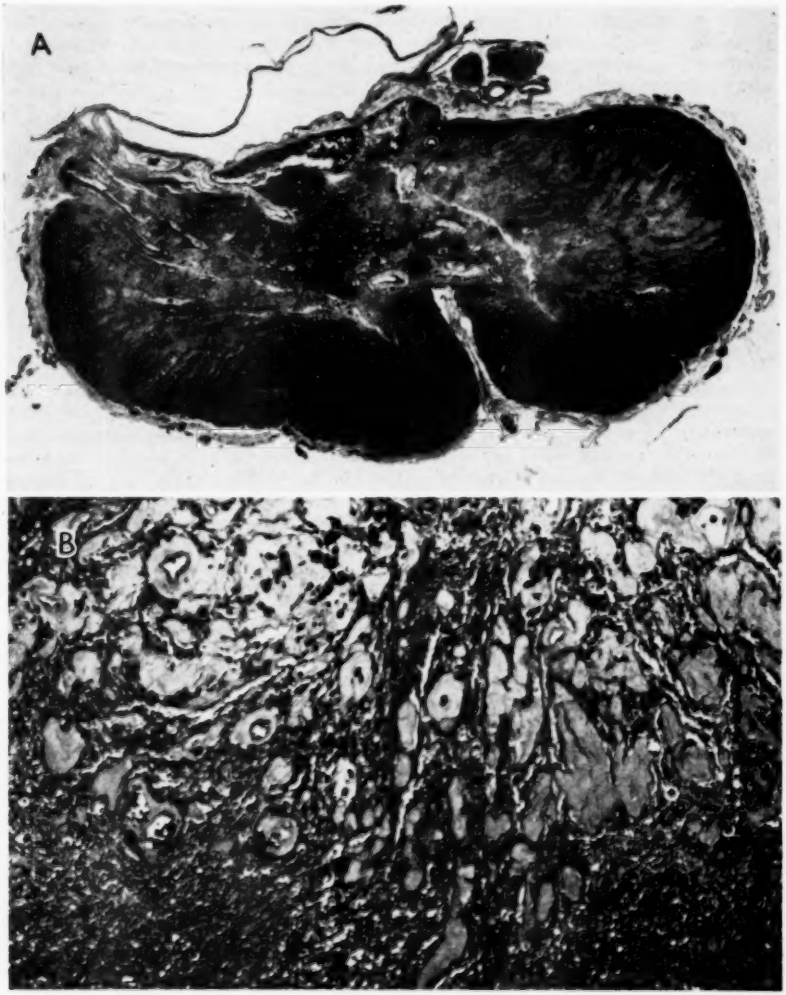

Fig. 7.—(*A*, Case 6) At the sixth thoracic vertebra the posterior half of the spinal cord is severely altered. Many clusters of small intraspinal malformed veins are present. × 27; Weil stain.

(*B*, Case 7) Clusters of malformed and thick veins are distributed in relatively well-preserved parenchyma at the sacral level of the spinal cord. × 120; hematoxylin-eosin stain.

addition, a typical old plaque of multiple sclerosis occupied one lateral tract and the adjacent portion of the gray matter. No abnormal vessels were seen in or around this plaque.

In the lower part of the medulla there was ascending demyelination of the fasciculus gracilis. A few abnormal veins were seen at this level. One pyramid contained a fresh hemorrhagic softening. Other demyelinated plaques were found in the floor of the fourth ventricle, in the restiform body, and scattered in the centrum ovale. There were no abnormal vessels either in the plaques or in the surrounding parenchyma.

Comment: The complexity of the anatomic lesions is the unusual feature of this case. The meningioma is without clinical significance, but two other lesions assume a large role in the neurologic picture. One was the venous malformation of the spinal cord and its coverings. The major lesion was focal, although minor forms were encountered at various levels. Secondary to this were two foci of malacia, one in the midthoracic region and the other in the medulla. The other lesion was the demyelinated plaque of multiple sclerosis. It is probable, in view of the history of pain and of the sensory changes on admission, that the onset of the disease was the result of the thoracic softening.

Case 7.—F. H., a white woman aged 25, during pregnancy in 1931 noted the onset of paroxysmal, nonradiating pain in the right buttock. The pain subsided spontaneously after delivery. Nine months later, a similar intermittent pain reappeared and radiated down the anterolateral aspect of the right thigh to the external malleolus, and upward to the base of the occiput. This was aggravated by coughing, and attacks lasted from a few hours to several days, with pain-free intervals of weeks or months. In 1933 weakness of the right leg appeared. Study at another hospital revealed a complete block of spinal fluid and a "defect" in the myelogram. A laminectomy from the 12th thoracic to the 3d lumbar vertebrae revealed a swollen spinal cord; large, congested vessels, and numerous yellow-purple zones of discoloration in the exposed area, mostly in its inferior portion. The diagnosis was intramedullary tumor with recent hemorrhage, but biopsy was not done. After operation, anesthesia of the right lower extremity, incontinence of urine, and weakness of both legs developed rapidly.

The patient received 23 deep x-ray treatments, with such improvement that she was able to walk until 1940, when, after a fall, paraplegia became complete. She was transferred to this hospital in June, 1941. Examination revealed flaccid paraplegia with atrophy of the right thigh, hypotonia, and absence of deep reflexes in the lower extremities. Cutaneous abdominal reflexes were also absent. The Babinski sign was not elicited. There was complete anesthesia up to the 11th thoracic dermatome on the right and the 1st lumbar dermatome on the left. There were urinary incontinence and decubitus ulcers. The upper limbs and cranial nerves were intact. There were no meningeal signs. Examination of the cerebrospinal fluid in July, 1941, revealed 29 red blood cells per cubic millimeter, 266 mg. of protein per 100 cc., a 2+ Pandy reaction, a negative Wassermann reaction, and a gum mastic curve of 2355532211.

In January, 1942, the cerebrospinal fluid contained 482 red blood cells per cubic millimeter, 300 mg. of protein, per 100 cc., a 2+ Pandy reaction, a negative Wassermann reaction, and a gum mastic curve of 3333110000. At this time the cerebrospinal fluid was xanthochromic, and there was a block after removal of 13 cc. of fluid. A myelogram showed delay of movement of the dye at the third thoracic segment and narrowing of the column from the third thoracic segment down.

The neurologic picture remained the same, but an ascending urinary-tract infection developed. The patient died in February, 1949, after a laparotomy for a right perinephric abscess. The duration of illness was 10 years from the onset of weakness and 18 years from the first episode of pain. The clinical diagnosis was intramedullary tumor of the spinal cord at the lumbosacral level.

Necropsy revealed chronic cystitis and operative absence of the right kidney.

The brain was normal. The spinal cord was shrunken, with complete replacement of the sacral region by an oval hemorrhagic mass, which measured 5 by 1.5 by 1.5 cm. Atrophic fibers of the cauda equina surrounded the mass. There were adhesions between the dura and the leptomeninges throughout the length of the cord, being more numerous in the sacral

region. Cysts in the gray matter and widespread demyelination were seen in the cervical and upper thoracic portions of the cord. Histologic examination revealed a tremendous increase in the number of blood vessels, chiefly within the sacral portion of the cord and partly around the fibers of the cauda equina. These vessels were both scattered and agglomerated in large clusters. They consisted of extremely thick, hyalinized veins with narrow, often occluded, lumens (Fig. 7*B*). Though less numerous, arteries with thick walls, split elastica, and calcification of the media were also seen. The parenchyma of the sacral portion of the cord contained areas of old and recent softenings, with disappearance of the normal structures and intense gliosis.

At the thoracic and cervical levels there was an ascending demyelination. In addition, glia-lined cavities were seen posterior to the normal central canal.

Comment: This young woman had a flaccid paraplegia of long duration, with a sensory level at the 11th thoracic dermatome. An interesting item is the long history of pain preceding the onset of paraplegia and its relation to pregnancy. Such pain is a common symptom in vascular anomalies. The findings at laminectomy were in support of this diagnosis, but the final answer came from necropsy, which revealed arterial and venous malformations of the lowest part of the cord with evidence of many successive hemorrhages. The vessels were not malformed at the level of the cavities in the thoracic and cervical portions of the cord. These cysts might have been due to associated malformation in the nature of syringomyelia, or perhaps they were related to roentgen therapy.

Case 8.—H. H., a white woman, fell on the lower end of her spine when 13 years of age, in 1921. Two years later kyphoscoliosis was first noted. In April, 1928, she complained of numbness in the umbilical region. One week later she experienced pain in the left side of the neck and radiating down the left arm to the elbow. The pain was accompanied by stiffness of the neck and slight difficulty in initiating the urinary stream. Three weeks after appearance of the pain there was onset of weakness and stiffness of the left leg. She entered another hospital in May, 1928, where a myelogram showed a block at the third cervical segment. A laminectomy performed between the fourth and the sixth cervical vertebra revealed adhesions between the arachnoid and the dura and swelling of the cord. A diagnosis of intramedullary tumor was made. She was transferred to this hospital in August.

Examination revealed spastic paraplegia, associated with flaccid paralysis and atrophy of both arms. The deep reflexes were absent in the right arm. There was dissociated sensory loss between the 2d and the 12th thoracic dermatome on the right and the 4th thoracic and the 1st lumbar dermatome on the left, with some sparing of touch sense. Sensation mediated by the posterior column was absent in the lower extremities. There was sphincteric incontinence. The neck was stiff. Lumbar puncture showed a manometric block. The cerebrospinal fluid was normal except for a 2 + reaction for globulin. The sensory loss later involved all modalities, and in 1929 the level reached the second thoracic dermatome. In 1930 the level was at the first thoracic dermatome, but with additional involvement of the right arm for pain with sparing of touch sensibility. Deep x-ray treatment did not alter the course. Cystitis and huge bedsores developed. She died in September, 1933, after a total illness of five years.

Only the cervical portion of the cord was removed for necropsy. The spinal dura was thick. The cord itself had a cystic, hemorrhagic appearance. The upper part was softened and appeared gelatinous, while the lower part contained a hemorrhagic cavity. On histologic examination, the center of the cervical portion appeared softened and necrotic and was surrounded by a peripheral shell of partially demyelinated nerve tissue (Fig. 8*A*). The central cavity, as well as its wall, contained many veins. These had thick, hyaline walls and greatly reduced lumens, and were frequently arranged in clusters of three or four (Fig. 8*B*).

Comment: This patient presented a clinical picture of intramedullary tumor of the cervical region of the cord. Actually, the pathologic process was extensive softening secondary to obvious anomalies of the intraspinal veins.

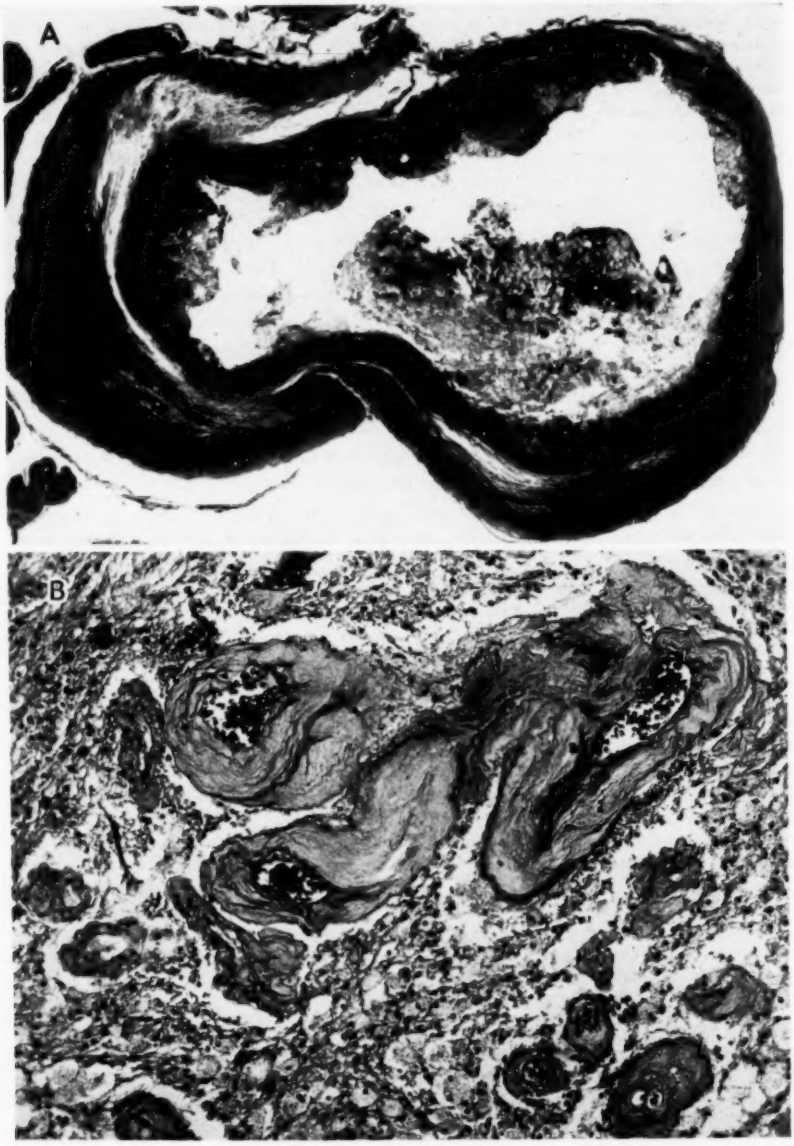

Fig. 8 (Case 8).—(*A*) Central softening of the cervical region of the spinal cord has resulted from an intraspinal venous malformation. The altered vessels are seen within and at the edge of the cavity. × 10; hematoxylin-eosin stain.

(*B*) Clusters of fibrotic malformed veins lie between areas of softened neural parenchyma. × 180; hematoxylin-eosin stain.

CASE 9.—M. F., a white man aged 67, noted the onset of pain in the lower part of the left shin in 1946. By 1947 there were paresthesias in the same area. In January, 1948, the pain extended to the left knee and ankle, while numbness of the right foot appeared. In July, 1948, studies led to a diagnosis of neuritis of unknown origin. Thereafter the pain increased; there were numbness in both feet and weakness and stiffness in the left leg. Neither back pain nor intermittent claudication was present. He was admitted to this hospital in August, 1949. Examination revealed distal paralysis of the left leg with exaggerated ankle jerk and absence of the knee jerk. There was a bilateral Babinski sign. Cutaneous abdominal reflexes were normal, but the cremasteric reflexes were absent. There were complete anesthesia from the fourth lumbar to the second sacral level on the left side and hypesthesia in the same territory on the right. Deep sensation was absent in the lower part of the left leg. There was sphincteric incontinence. The lower part of the spine was rigid. Lumbar puncture did not reveal block. Examination of the cerebrospinal fluid revealed 3 lymphocytes per cubic millimeter, 32 mg. of protein per 100 cc., and a negative Wassermann reaction. A myelogram revealed nothing abnormal.

During the subsequent months the sensory level remained the same, but both legs became equally involved, with clonus of both ankles, absence of the left knee jerk, and diminution of the right knee jerk. A myelogram, repeated in October, revealed a narrow column at the 12th thoracic-first lumbar level. A thoracolumbar laminectomy in November revealed a discolored lumbar area of the cord, under a thickened arachnoid. The cord appeared firm and swollen with brown cystic areas on its surface. A puncture gave issue to greenish fluid and old blood clot. Abnormal tissue was seen, but the surgeon considered the removal of a biopsy specimen too dangerous. The patient's neurologic condition after operation remained unchanged. He had an episode of unexplained bleeding from the urinary tract and septicemia, which responded to antibiotic therapy. He was recovering from the latter when he suddenly became cyanotic and pulseless and died, in January, 1950. The duration of neurologic disease was six years. The clinical diagnosis was intramedullary tumor of the cord with hematomyelia.

Permission was obtained only for examination through the operative incision. The lower part of the cord, from the third thoracic segment to the conus, was removed for study. The posterior surface of the dura was thickened, as a result of the operative procedure. A few small, old hemorrhages were seen on the inner surface, and some filmy adhesions were present between the dura and the arachnoid. The thoracic segments had a normal appearance. In the lumbar enlargement there was almost complete replacement of the parenchyma by a hemorrhagic mass, which was surrounded by a capsule (Fig. 9*A*). This mass was 0.75 cm. in length. The hemorrhage was entirely intramedullary. There was no blood in the conus or around the roots.

Histologic examination revealed that one-half of the lumbar portion of the cord was replaced by a large, blood-containing mass. This was composed of a fresh clot with early organization. It was lined by a thick, wavy wall of hyaline connective tissue, which was calcified in spots and contained foci of atheroma. Serial sections revealed a few outpouchings with replacement of the wall and lining by newly formed connective tissue. In the upper portions there was a separation into two parts: One was an empty, thick-walled, enlarged channel, and the other, an organizing thrombus, surrounded partly by a thick, hyaline wall of connective tissue (Fig. 9*B*). The anterior spinal vein was thick and enlarged and was continuous with a thick, large, tortuous sulcal vein. Though direct communication was not seen, it is probable that the pouch inside the cord was connected with this anterior sulcal vein. Around the mass in the cord were many dilated and thick veins lying isolated or in clusters; some of them occupied positions in the wall of the pouch. There were many hemosiderin-laden macrophages, lymphocytes, and plasma cells.

The other half of the cord was in large part compressed but contained several clusters of abnormal veins. Around the cord there were several malformed veins, the most conspicuous being the anterior spinal. Arteries, especially the anterior spinal, had a proliferated subendothelial layer. The spinal cord above and below the lesion was secondarily demyelinated.

Comment: The clinical picture in this case was one of leg pain during the first three years. It was only during the last three years that the addition of progressive spastic paraplegia with a sensory level led to laminectomy and to the diagnosis of intraspinal tumor with hematomyelia. The spinal lesion, however, was secondary to destruction of one-half the lumbar portion and compression of the other half

by a hemorrhagic mass. This mass was formed by an enormously dilated vascular channel with secondary outpouchings, ruptures, and organization of the resulting hematomas. In addition, a number of small, malformed veins surrounded the large pouch. The walls of the dilated pouch were thicker than the malformed veins and

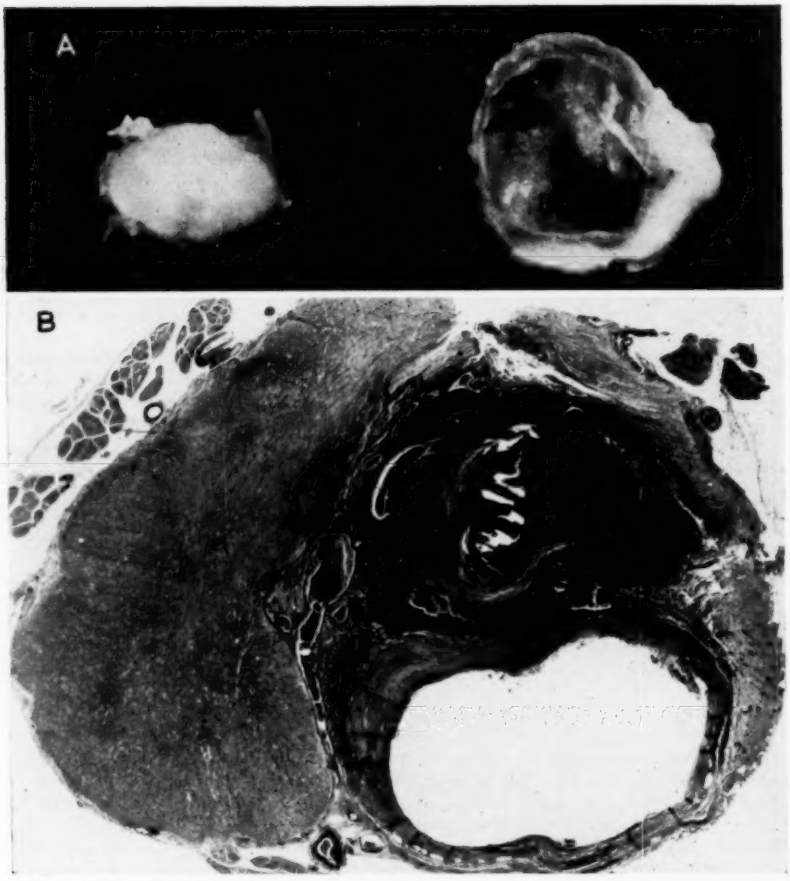

Fig. 9 (Case 9).—(*A*) The normal thoracic spinal cord is on the left. The pouch of the arteriovenous aneurysm in the lumbar region is seen on the right, replacing a portion of the cord. (*B*) The dark mass above is the result of rupture of an outpouching from the large aneurysm seen below. In addition, there are small malformed veins, which lie medially. × 6; Weigert stain.

were atheromatous. Such a structure is unusual, and the mechanism of formation is unknown. It is conceivable that this structure represents part of an arteriovenous aneurysm, but a communication between it and the anterior spinal artery,

or any other arterial vessel, was not demonstrated. Arteriovenous aneurysms which involve the spinal cord have been reported in only four instances.[9]

GENERAL COMMENT

Both focal and diffuse vascular malformations of the spinal cord are not easy to diagnose on clinical grounds. In the diffuse form the following facts are helpful: the apparent frequency in males of middle age; onset with pains preceding the paraplegia by a variable period; occurrence of successive episodes at the same levels; clinical succession of spastic, then flaccid, paraplegia, with secondary disappearance of deep reflexes and the Babinski sign, while the paraplegia ascends, and, finally, dissociated sensory loss, with slow ascent of the sensory level and late appearance of complete anesthesia. In the cases reported here, the first stages of spastic paraplegia and of dissociated sensory loss were lacking, perhaps because the patients were seen at Montefiore Hospital late in the course of their disease. The common feature which remains in these cases is the presence of severe flaccid paraplegia.

In the more localized forms similar onset with pain and recurrent neurologic signs may be encountered. Here the disease occurs as frequently in females as in males. Moreover, the picture is nonspecific, being that of a spastic transverse "myelitis." The association of vascular anomalies in the skin also has been pointed out as a diagnostic hint, but frequently is absent.

The appearance in the cerebrospinal fluid of many red blood cells and an increase in protein content is helpful, but is inconstant. The myelogram rarely shows a characteristic picture. The commonest finding is a simple delay in passage of the dye or its complete stoppage. Shadows with smooth, parallel, curvilinear sides, which represent the tortuous vessels surrounded by contrast substance, were described by Guillain and Alajouanine,[10] and recently by Epstein and Davidoff.[11]

Even laminectomy permits the diagnosis only in cases in which there are abnormal vessels in the leptomeninges, but not when the malformation is intraspinal. It is difficult to decide correctly by direct observation the type of vessel involved in the malformation.

The duration of illness in this series ranged from 3 to 13 years, with an average of 7 years. The age of onset was from 13 to 67 years. The course was always slowly progressive.

Pathologically, the diagnosis is easy, and the picture is that of the characteristic malformed vessels with myelomalacia. The vessels may be either veins or arteries, or, more frequently, both veins and arteries. These pathologic variations do not have clinical significance. As already pointed out, the only important clinicoanatomic correlations depend on whether the lesions are focal or diffuse. The distribution of the vascular lesions in our nine reported cases is shown in Figure 10.

9. (*a*) Brasch, F., cited by Wyburn-Mason.[5] (*b*) Frey, L.: Étude anatomo-clinique d'un cas d'anévrisme cirsoïde de la moelle épinière, Ann. anat. path. **5**:971-979, 1928. (*c*) Robertson, E. G.: A Case of Arterial Angioma of the Spinal Cord, M. J. Australia **2**:384-385, 1938. (*d*) Guizetti, P., and Cordero, A.: Cited by Globus and Doshay.[1c]

10. Guillain, G., and Alajouanine, T.: Cited by Frey.[9b]

11. Epstein, B. S., and Davidoff, L. M.: The Roentgenologic Diagnosis of Dilatations of the Spinal Cord Veins, Am. J. Roentgenol. **49**:476-479, 1943.

The cases of the diffuse type (Cases 1 to 5) are similar to those reported by Foix and Alajouanine and by others.[12] In our opinion, subacute necrotic myelopathy is secondary to diffuse vascular malformations.

The malformed vessels have a few basic characteristics. They are increased tremendously in number and size, and the walls usually are much thicker than those of normal vessels. They frequently are arranged in clusters of two to five. Meninges or nerve tissue, normal or altered, is generally seen between them. There are numerous secondary modifications, such as thickening of the walls, hyalinization, and the presence of organized thrombi with partial or complete occlusion. The thrombi, in large part, are responsible for the softening of the cord.

These characteristics help to separate malformations from other lesions. The differential diagnosis includes old inflammatory changes in the spinal cord. These

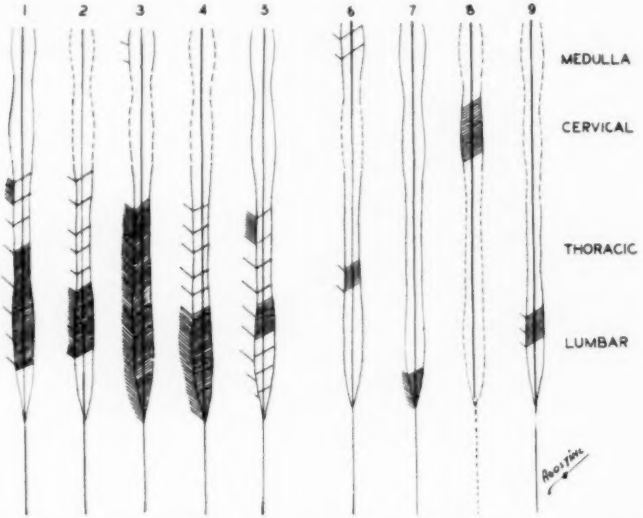

Fig. 10.—Diagram illustrating the severity and distribution of the vascular alterations in the nine cases. Heavy shading indicates a severe malformation; light shading, a mild one. The shading to the left of the spinal cord demonstrates meningeal distribution; the intramedullary lesions are shown within the cord. Those portions of the central nervous system not examined are shown by dotted lines.

processes may result in capillary proliferation but are not accompanied by increase in the number of large vessels. Structural alterations of previously normal vessels, as in arteriosclerosis, must also be differentiated. In these cases the vessels are reduced in caliber or are thrombosed, have thick walls, but are not arranged in clusters and are not increased in number. A third type to be eliminated are cases with epidural compression of vessels leading into the cord. In these instances, the vessels, especially veins, are hugely dilated, and the walls are thinner than usual.

12. Footnote 3. Wyburn-Mason.[5] Stolze.[6]

Embryologic Development of the Vessels of the Spinal Cord.—In order that the origin of malformed vessels during development may be understood better, a brief résumé of the embryology of vessels of the spinal cord is given.[13] The early vascularization of the cord is furnished by the dorsal segmental vessels, which arise from the aortae during the fifth week of embryonic life. These dorsal segmental arteries and veins appear at first in the cranial end of the embryo of two somites, then arise progressively more caudally until they attain the number of 30 pairs. The segmental arteries divide into several capillary branches, two of which become enlarged, forming at each segment, the dorsal and ventral radicular arteries. These capillaries sprout to cover the lateral surface of the cord with an anastomotic net. The medial part of the anterior surface and the posterior surface are entirely avascular. The medial margin of the capillary net enlarges and gives rise to two longitudinal vessels, one on each side, which are the primitive anterior spinal arteries. The anterior radicular arteries play, of course, the principal role in the formation of the latter. From the anterior spinal arteries arise sulcal arteries and numerous capillary bridges which cross the anterior surface of the cord.

It is in the embryo of 7 weeks that a single anterior spinal artery is first seen. This is the result not of a fusion but, rather, of a selection of one of the various pathways offered by the two primitive anterior spinal arteries and the capillary plexuses between them. This explains variations in position of the definitive anterior spinal artery, which may be median, lateral, or oblique.

After formation of the anterior spinal artery, similar anastomoses of the posterior radicular arteries give rise to two symmetrical posterior spinal arteries, which then vascularize the posterior surface. The gray matter is the first to receive an irrigation, which comes principally from the sulcal arteries. The white matter becomes vascular very late.

Venous trunks develop during the same time, and in exactly the same order, as the arteries. While the development of the vessels reaches its final point, primitive trunks and capillary nets disappear progressively. The segmental vessels become associated more and more with the skin, principally, the myotomes, so that the radicular arteries, which were first to develop, appear later chiefly as collaterals. Furthermore, many of these radicular arteries become atrophic, so that only a few reach the definitive anterior or posterior spinal arteries, and the spinal vascular supply loses its primitive segmental character.

In the adult cord[14] the anterior spinal artery is supplied only by six to eight nonpaired radicular arteries, the largest one being at the third lumbar level, the arteria radicularis magna. The posterior radicular arteries joining the cord are, similarly, only five to eight in number and do not give rise to a continuous posterior spinal artery.

The anterior spinal vein is formed by 6 to 11 anterior radicular veins, and the large posterior spinal vein is formed by vertical anastomosis of 5 to 10 posterior

13. Minot, C. S.; Evans, H. M.; Tandler, J., and Sabin, F. R.: Development of the Blood, the Vascular System, and the Spleen, in Manual of Human Embryology, edited by F. Keibel and F. P. Mall, Philadelphia, J. B. Lippincott Company, 1912.

14. Suh, T. H., and Alexander, L.: Vascular System of the Human Spinal Cord, Arch. Neurol. & Psychiat. **41**:659-677, 1939.

radicular veins. The vascular supply is rich in the cervical and lumbar regions, while the zone of poorest circulation is in the midthoracic segments.

The complexity of this development may help to explain the occurrence of malformations. These are due to the use of unusual pathways in the primitive plexuses and to the persistence of vessels normally obliterated during development. The last possibility may be confirmed in normal persons by the finding of a normal spinal artery side by side with two or three malformed vessels (Fig. 11). A few hypotheses concerning the malformations discussed here are suggested from this developmental study:

1. The almost parallel development of arterial and venous circulation explains the frequency of malformations involving both types of vessels.

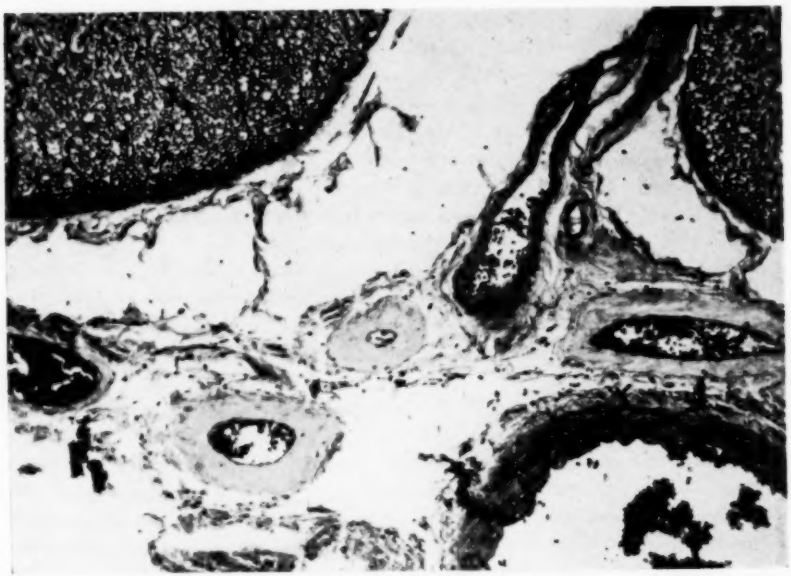

Fig. 11.—Anterior sulcal region in a normal subject. Malformed blood vessels lie between a normal anterior spinal artery and a normal sulcal vein. × 120; hematoxylin-eosin stain.

2. The later vascularization of the caudal part of the spinal cord and of the posterior surfaces may explain the greater frequency of malformations in these regions, since any causal agent has a greater length of time in which to act, or, alternatively, more time is allowed for errors in development.

3. The various types of vascularization, first segmental, then plurisegmental, and, finally, diffuse, may account for the two types of malformation: first, the diffuse and nonsegmental malformation, which generally involves the lower half of the cord; and, second, the focal variety, which is composed mostly of intraspinal lesions.

SUMMARY AND CONCLUSIONS

A surprisingly high percentage of vascular malformations of the spinal cord was encountered in a large series of cases of "myelitis" with necropsy.

The cases reported can be divided in two groups: In one, with diffuse lesions, the malformation generally results in flaccid paraplegia and occurs mostly in middle-aged men. The Foix-Alajouanine syndrome of "subacute necrotic myelopathy" is believed to be secondary to such lesions. In the other group there is a focal lesion with a nonspecific picture of transverse myelitis, resulting in spastic paraplegia. Focal lesions are seen with equal frequency in both sexes and at all ages.

Anatomically, the basic lesion in both groups is a vascular malformation with secondary destruction of the cord by softening. This malformation involves most frequently both veins and arteries, within both the cord and the leptomeninges. Rarely it involves only veins or arteries, but this is not clinically significant. The lower parts of the spinal cord are more frequently involved. There are no correlations between the site or extent of the lesions and the type of vessels involved. The distribution of the process alone accounts for the clinicopathologic picture.

The embryologic basis of spinal vascular malformations is reviewed.

Mr. Antol Herskovitz prepared the photomicrographs.

A STUDY OF THE SYNDROMES OF DENIAL

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IN THE neurological literature are recorded experiences with many patients who denied parts of the body or dysfunctions of various parts. The classic, or topographical, approach to the denial syndromes has been summarized by Roth [1] and examined further by Sandifer.[2] Schilder dealt with these phenomena in terms of the patient's body image.[3] More recently, Weinstein and Kahn [4] have presented a study of "anosognosia," broadening its definition to include denial of many defects of function and of events in the patient's recent experience, such as operations. The various phenomena of denial are linked together by these authors as manifestations of a defensive psychological attitude temporarily adopted by the patient with gross structural defects of the central nervous system as a means of immediate protection against the recognition of life-threatening disease processes. According to these authors, the premorbid personality is characterized chiefly by perfectionistic trends.

Two patients recently admitted to the neurological service of this hospital have demonstrated denial syndromes. An investigation has been made of the premorbid personality and attitudes of each patient in their relation to the development of this syndrome. A means of testing their responses to experimentally induced defects in function has been studied.

CASE 1.—The present admission was the first of a 40-year-old, right-handed, married white woman, a housewife and mother of three children, who was brought here by her husband on Oct. 1, 1951, because of unsteady gait of one year's duration and headache for one month.

The history on admission was obtained from the husband. He had known the patient for one year prior to their marriage, in 1947. During this time she was cheerful and appeared to him normal in every way. When they returned from their honeymoon, she refused to cook meals and seemed to walk more slowly than previously. At this time there was loss of sexual desire, which persisted up to the time of the present admission. Within six months of marriage

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1. Roth, M.: Disorders of the Body Image Caused by Lesions of the Right Parietal Lobe, Brain **72**:89-111 (March) 1949.

2. Sandifer, P. H.: Anosognosia and Disorders of Body Scheme, Brain **69**:122-137 (June) 1946.

3. Schilder, P.: The Image and Appearance of the Human Body: Psyche Monograph 4, London, Kegan Paul, Trench, Trubner & Co., Ltd., 1935.

4. Weinstein, E. A., and Kahn, R. L.: The Syndrome of Anosognosia, Arch. Neurol. & Psychiat. **64**:772-791 (Dec.) 1950.

she became careless of her person, irritable, and forgetful. She seemed to be "in a daze" and would forget to flush the toilet after using it. These changes were progressive, so that in the past year the children and apartment were frequently neglected. She was extremely quarrelsome with her neighbors. She had been noted to blink her eyes excessively and for three years had had blurring of vision while watching television. There had been no diplopia or blindness. Her speech had been low, almost inaudible, slowed, and stuttering for a year. She had also complained of "dizziness," i. e., a sensation that she was about to faint, for one year. In 1951, nine months before admission, and shortly after the uncomplicated delivery of her third child, she exhibited unsteadiness of gait. Six months before admission she fell while carrying her baby in the street. For three months before admission she complained of "numbness" of the entire left side of her body. One month prior to admission she began to complain of nonfocal headache, which was relieved by acetylsalicylic acid. On the day before admission she awoke on the floor with her baby beside her.

Past History.—The patient had sustained a head injury in a fall from her bunk while in the WAVES, in 1943. There was unconsciousness for an unknown period, but no sequelae.

In April, 1944, she entered a United States naval hospital with the complaint of inability to taste and numbness and paresthesiae of the left side of the face of one week's duration. On physical examination, she showed slowness in answering questions, a lack of facial expression, weakness of the left lower part of the face on smiling, decreased sensation for pin prick and cotton over the left side of the face, and impaired taste sensation on the anterior portion of the tongue. Because of her mother's death, she was given leave, and upon her return, several weeks later, all the symptoms and signs had disappeared.

Past Personal History.—The patient was one of eight siblings, whose father deserted them when the patient was a young child. The mother was described by the patient as "the brains of the outfit" and apparently was an excellent business woman, being able to support and rear her children without remarrying. The mother, however, regretted never having had any twins and frequently said, "I so wanted to have twins." Accordingly, the patient and her younger sister, Elizabeth, were dressed as twins, used a twin's perambulator, and slept in the same bed. The two little girls were called "the twins" by the family.

According to the patient, she has always been sorry not to have been one of a pair of twins because "twins get more attention." She always felt there were great differences between her and Elizabeth. "She was as different from me as night from day. I was as light as she was dark. She was always getting dirty. I never played with the dirt; my hair showed the dirt; hers didn't. Elizabeth was the one that was bad. It seems as if two is so much more than one—they are heavenly. My dolls have always been twins."

The patient was sent to parochial school, where the Sisters made everyone use his right hand. "They told us how hard it was to use the left hand. Of the children in the class, two were left-handed. They were both 'naughty' and 'bad.' The Sisters used to punish them." Because of an episode of playing with one of the left-handed girls, in which a piece of doll furniture was broken, the patient was severely punished by her mother. The Sisters taught the children that "the right hand was to be used in the later life."

After finishing high school and two years of business college, the patient went to work as a clerk. Meanwhile, her "twin" sister, Elizabeth, had gone into the Orders, finally being sent to do missionary work in Samoa. The patient stated, "I should have been the nun. I was good; Elizabeth was bad, always getting me blamed for her mischief. The Sisters don't have it so bad."

During service in the WAVES, the patient married a high-ranking officer. "He was swell; he treated me like a baby, like a doll. He was so good to me." This officer was killed in an airplane crash. Meanwhile, the patient had been discharged and bore a posthumous child. After a period of time with her family again, working as a clerk, she remarried, this time a printer. Toward this, her present, husband she expressed much affection, but he "wasn't as nice to me" as the first husband. With this husband she had two more children.

The patient remembered having had difficulty with her left hand only since her fall in 1943. In 1944 and 1947, for several days, the left hand felt weak and "as though it didn't belong to me." Again, "It caused me all the trouble, too limp. I'll have to watch it more carefully. It's a sad me, but it's me."

She further expressed a regret that her own children, especially the younger girl, had not been one of twins. She stated that she often dressed the younger boy and girl as twins.

The patient said that two days before admission she "went to pieces" during her youngest child's first birthday party, this event being the last thing she could remember before admission. "I don't know why, but I put two candles on the cake. I was bringing the cake in. Then the baby tried to blow out the candles. That's all I remember."

Physical Examination.—At the time of admission, she was small, pale, and normotensive, with a pulse rate of 48 a minute. General examination revealed nothing unusual except for a Grade-2 systolic murmur at the cardiac apex, which was transmitted upward.

The patient was depressed and apathetic. Denial of the left side of the body is described separately. Simple calculations were done well, but very slowly. More complex calculations and serial seven's were done poorly. The patient did not know the day, date, month, or year. ("About 1948 or 9.") She said the season of the year was "school time." When told it was October, she replied, "What happened to September?" She knew she was in a hospital but could not supply the name or location. She had no idea of how she came to be in a hospital and could not remember events of the previous evening. Her memory for remote events was poor. She had a mixed aphasia and read very slowly by spelling out letters. Some objects could not be selected upon reading their names, even when read correctly.

The patient walked with a halting, staggering gait. Smell sense was absent on the left. Both visual and auditory stimuli on the left were referred to the right side. In addition to left homonymous hemianopsia, there was bilateral end-gaze horizontal nystagmus. Sensation for pin prick and cotton was impaired or absent on the left side of the face, and pin prick was sometimes referred from the left to the right side of the face. The tongue protruded in the midline but could not be moved to the left. Speech was slurred and stuttering. The head could not be turned to the left.

There was weakness of the left shoulder and arm, with finger-to-nose ataxia and a forced grasp on the left. The strength of the left arm improved with suggestion. There were no reflex changes in the arms. Whereas in the right arm sensation was intact, all forms of sensation were impaired or absent in the left arm. When perceived, a stimulus on the left was sometimes referred to the right arm.

The superficial abdominal reflexes were absent. There were weakness, ataxia, and decreased rapid rhythmic movements of the left lower extremity, with great variability in performance. There were no definite reflex changes, but an abnormal plantar response was found on the left side. There was no sensation in the left leg except for intact position sense. Perianal sensation was decreased on the left.

Motor performance on the left side seemed to improve with suggestion as the examination progressed. At the end of the examination the strength in the left extremities was almost equal to that in the right.

On double simultaneous stimulation of the left and right sides of the body in homologous areas, only the stimulus applied to the right side of the body was perceived. However, when the left side of the face and the left arm were simultaneously stimulated, a single stimulus was sometimes felt on the left side of the face.

When asked to move the left side of the body, the patient moved the right side. When first questioned, she denied the existence of the left side of the body. When confronted with the left hand, she said it was not her hand but the examiner's. The following is a record of the conversation held with her at this time:

"Where is your right hand?" (Holds up her right hand.)

"Where is your left hand?" (Hesitates. Looks about her and appears uneasy. Raises her right hand again.)

"This is your right hand." (Examiner holds her right hand before her.) "Now, everyone has two hands. Where is your other hand?" ("I don't know.")

"Whose wedding ring is this?" (Examiner points to ring on third finger of patient's left hand.) (Answer: "My ring.")

"And whose hand is the ring on?" ("On your hand. That's not my hand; that's your hand. You must have taken my ring.")

The same procedure was then repeated for the feet, the shoes being used as identifying symbols. The results were the same as those for the hands. The patient maintained that the left shoe was on the observer's foot and not her own.

Laboratory Examinations.—The results of a complete blood count, urinalysis, serologic tests, and blood sugar and urea determinations were normal. Lumbar puncture showed clear fluid under normal pressure, and laboratory studies of the fluid revealed nothing unusual. Visual-field studies revealed no defect. Roentgenograms of the skull and chest and intravenous pyelograms showed nothing abnormal. An electroencephalogram, on Oct. 3, 1951, was reported as a "grossly and diffusely pathological record." Psychological testing over a three-week period was performed. A summary of these tests is as follows:

"This woman, who has been a person of above average intelligence, is now functioning at a child-like level of adjustment. Intellectual control is markedly impaired, with many indications of disordered and autistic thinking. There are an attempt to repress all the unpleasant aspects of reality and a strong longing for a carefree, happy, center-of-attention kind of life, which we usually associate with children. The passive, dependent needs and the extreme emphasis on repression point out the hysterical features of her make-up. However, there are other aspects of her functioning which are usually associated with structural brain damage. While there can be little doubt as to this woman's psychosis, it is not possible to classify it more specifically on the basis of the psychological test."

Hospital Course.—During the first few days of hospitalization, there was remarkable improvement in many spheres of functioning on no therapy other than modified bed rest and frequent interviews, during which much solicitude was expressed and encouragement given. Four days after admission the patient was smiling, responding to jokes with laughter, and expressing concern about her condition. Orientation and recent memory were still poor, but she spontaneously recalled an episode of her previous marriage when asked to tell something about herself. Aphasia had disappeared. Gait was moderately improved. Tubular vision was present. Nystagmus, auditory and visual allesthesia, and the denial syndrome were no longer present. When questioned about the left side of her body, she no longer referred to it as belonging to the examiner, but said, "He's mine, but something is wrong with him. He's not so good." And, again, "This side (pointing to the right) is good, and this side (pointing to the left) is bad. The bad side is dragging me down."

Special Studies.—When examined on Oct. 4, 1951, the patient had no aphasia in tests using common objects. There were no defects of reading, writing, spelling, or simple calculations.

A. Directions: The patient was able to point up, down, right, and left. She identified clockwise and counterclockwise. When shown North, she properly identified other points of the compass.

B. Distances: She described the ceiling as 7 ft. (2 meters) high (actually, 14 ft. [4.3 meters]), but correctly judged a magazine to be 14 in. (35.5 cm.) long and the examiner's hands to be 1 yd. and 1 in. (91 and 2.5 cm.) apart, respectively, on two estimations.

C. Simple Geometric Forms: She was able to draw a triangle, a circle, a square, a rectangle, and a parallelogram correctly with the right or the left hand. She was able to form a circle, a triangle, and a square, using the right and left index fingers and thumbs. She was unable to name these forms correctly.

D. Finger Designs: Using both hands, she was able to imitate correctly complex interpositioning and interlocking of fingers, as demonstrated by the examiner.

E. Straight Lines: She was able to recognize on a piece of paper with many lines on it, which lines were straight and which were curved, which of two lines was longest, but not which were parallel.

F. Simple Drawings: She was able to draw correctly, using the right hand, an automobile and a bicycle.

G. Orientation: She was able to identify the location of her room correctly and its relationship to the hall. She said it was "9 p. m." (actually 4 p. m.).

H. Right and Left: Although able to identify her own right and left sides, she was incorrect in identifying the examiner's right and left hands.

I. Body Parts: Although incorrect about right and left, she was able to name correctly various parts of the examiner's body. She was also able to point these parts out on her own body. When directed, "Show me your . . . (name of body part)," she correctly touched all parts on the right side and could show her left eye. For left-sided parts thereafter, she would

touch the corresponding body part on the right side first, then proceed correctly to the corresponding part on the left. On one occasion, the left arm being under the pillow above her head, she was not able to find it. She became very anxious, saying, "It's opposite here somewhere." She finally located her left arm, with an expression of great relief. When a body part was touched and she was asked to name it, she performed perfectly for the right side. For the left side she described each part with such expressions as, "the other one," "the other belly," "my other toes." She identified the fingers of the left hand only by looking at, and repeatedly touching, the fingers of the right hand. When told to move the right and left body parts, she did so with ease on the right side but substituted right-sided for left-sided movements of the arms. Following directions given for movement of the left hand, fingers, or legs, she first moved the right extremity concerned, looked to the right, then looked to the left, and finally gave the correct motion for the left side. When asked, "Is this part yours?" she said "Yes" for all parts indicated. However, with the eyes closed, when the left leg was touched, she said, "Yes, that's mine," pointing to the right leg. When asked, "Is this part OK?" she said "Yes" for all parts on both sides with the following exceptions: For the left arm, hand, leg, and foot, she said, "He's slow, he's stiff."

J. Use of Hands: She was able to turn on a flashlight, demonstrate the use of a spoon, and make designs in the air, using both hands.

During the first 10 days of hospitalization, the patient improved remarkably. She became alert and affable, was overdramatic, and anxious for praise and encouragement, to which she reacted with great pleasure. She became oriented for time and place, still, however, showing defects in recent memory, especially as concerned the period just before admission. The aphasia, extinction, visual and auditory allesthesia, nystagmus, left homonymous hemianopsia, and left-sided sensory defect cleared completely.

Her gait became normal except that it remained slow. The weakness and ataxia of the left arm and leg also disappeared except for some awkwardness in using the left hand when following commands of the doctors or nurses. The superficial abdominal reflexes remained absent. The deep reflexes became hyperactive in the left arm and leg. A positive Babinski response was usually present on the left.

As she improved clinically the electroencephalograms were done serially and showed less slow activity, however remaining abnormal principally on the left side posteriorly. A record taken just prior to the air studies revealed that the maximum defect had now shifted to the right hemisphere.

Sodium-Amobarbital Interview.—This was done on Oct. 24, at a time when there was no denial of the left side. Under the influence of amobarbital (amytal®), the patient again referred to her left side as "He." When asked why, she said, "Because men are bad." This was quickly changed to "Some men are bad." After recovering from the amobarbital intoxication, she ceased referring to the left side in such terms once again.

Pneumoencephalogram.—This procedure, done on Nov. 5, 1951, was reported thus: "There is considerable dilatation of the body of each ventricle with no displacement from the midline. The subarachnoid markings in the temporal areas are dilated. The remainder of the ventricular system appears normal. The findings suggest rather extensive white and grey atrophy of the brain."

After the pneumoencephalogram, the patient appeared apathetic and sometimes mumbled incoherently. At times she was disoriented. She became incontinent of urine, but denied wetting herself. In addition, her gait again became unsteady. After one week, she stated for the first time that she was uncomfortable because she wet the bed. No denial of the left side returned.

Within another two weeks, the patient returned to her prepneumoencephalographic status, with clearing of all defects except for left-sided hyperreflexia, a Babinski toe sign on the left, and memory defects. Incontinence of urine disappeared.

The patient's status remained unchanged. The diagnosis at discharge was "cortical atrophy, diffuse, cause undetermined." At follow-up examination three months later the patient appeared more careless of her personal appearance than at the time of discharge. Her husband reported that she remained uninterested in domestic duties and seemed very forgetful. He stated that she had been intermittently incontinent of urine and feces. Neurological examination revealed nothing abnormal except for disorientation for time and memory defects.

CASE 2.—T. L., a 60-year-old, right-handed white man, a bank clerk, entered the hospital for the first time on Sept. 12, 1951, complaining of behavior changes of two weeks' duration.

At the request of his wife, the patient had abstained from alcoholic beverages while on a vacation six weeks before admission. He went to see his local physician with the complaints of diarrhea and mild substernal pain radiating into both arms. An electrocardiogram showed a myocardial infarction of the posterior wall. There was no evidence of cardiac failure, but the patient was placed on bed rest for a six-week period. While at rest three weeks before admission he experienced a severe bifrontal headache, nausea, and vomiting, together with drooling of saliva and weakness of the left arm. These symptoms came on suddenly. One day later he had a generalized convulsion, after which his left arm became weaker. After admission to another hospital the patient was observed to be "delirious and blind." A striking change in behavior was noted. He seemed to have marked memory defect. If unable to remember, he was noted to "make up stories." He had been having visual hallucinations, which included seeing his dead mother. He was reported to have had difficulty in walking and was observed to walk into the wall. He dropped things from his left hand. There had also been urinary incontinence.

Past History.—The patient had been a chronic alcoholic for many years. He had been having crampy pains in both calves at night for the past year. He had lost 15 lb. (6.8 kg.) in the month preceding admission.

Past Personal History.—The patient remembered his grandmother, who lived with his family in early childhood, as having been blind. She had been quiet, kindly, "very good to me," and "I also felt very sorry for her." "To me, blindness has always been the worst possible thing. I can never even look at a blind man, or any other sick man." Or again, "To me, blindness is the worst thing in the world."

Throughout a long and childless marriage the patient was rarely ill, but, as his wife described him, he was always apprehensive about becoming ill. A minor respiratory infection would require several days of rest in bed with the vigorous use of several medications. The only remembered illness occurred when he burned his right hand severely in hot water. Although he had suffered a third-degree burn, he looked at the affected hand, said it did not hurt, and refused medical aid until hours later, when his wife called the doctor over his strong protests.

Toward his wife's illnesses the patient adopted the attitude of trying to minimize any symptom of which she complained. His recurrent refusal to recognize that she was ill was responsible for a long delay in appendectomy early in their married life.

To sickness in all other people he responded with great concern, but refused to visit sick people.

In his business and personal life the patient was meticulous and punctual and demanded perfection in all he did. At a large bank where he handled correspondence, he was regarded as a most dependable employee.

Physical Examination.—At the time of his admission, general physical examination revealed a thin, elderly white man who was lying in bed. He was edentulous and normotensive. The dorsalis pedis pulses could not be felt on either side.

Neurological examination showed that the patient was disoriented for date and time of day, but knew his name and knew that he was in a hospital. He seemed anxious to join in a conversation. His mood was cheerful. There was a great deal of seemingly purposeless movement of the right upper extremity, and he continually attempted to sit up in bed.

The patient stated that he was in a hospital because he was having "trouble with my eyes." He was able to remember some of the details of his present illness. Recent memory was impaired. Remote memory was good. Simple calculations were done well; serial seven's were done poorly. The patient responded readily to suggestion with confabulation. There was no dysphasic disturbance. Information and recall were normal. The patient was anxious to return to his job at the bank.

The patient stood unsteadily, continually groping for support. He was unable to walk alone.

He had no light perception in either eye. The optic fundi were normal except for arteriolar narrowing. He was unable to look up, down, or to either side on command. There was weakness of the left lateral rectus muscle. The right pupil was larger than the left, but both pupils reacted to light directly and consensually and also reacted to near vision. There was hypesthesia of the left side of the face. There was no weakness of the face or tongue.

There was weakness of the left arm, with decreased resistance to passive stretch, impaired rapid rhythmic alternating movements, impairment of skilled movements, and poor check and rebound function. Tendon reflexes were increased in the left arm. There was a hemisensory defect on the left. In the arm this included perception of pinprick and cotton, two-point discrimination, position and vibration sense, figure writing, and point localization. He was unable to recognize common objects in the left hand. On the trunk the sensory defect included sensibility for pinprick and cotton. In the left lower extremity there were slight impairment of perception of pinprick and cotton, and vibratory sense, and deep pain and position sense, but no motor defects. There was no incontinence.

Additional Observations on Admission.—The patient was completely blind except for questionable light perception; yet he completely denied being unable to see. He repeatedly said, "There is nothing the matter with my eyes."

When asked to point to the window, he would point incorrectly and say, "There it is." When fingers were held before him, he would give a wrong answer but insist that he saw them. When an object, a hand, or nothing at all was held before him, he would describe a particular object, always incorrectly. "That's a book," "a light bulb," a "flower," etc. He would state positively whether the room light was off or on, usually incorrectly, but with great conviction. When asked to describe someone in front of him, he would do so incorrectly, but in minute detail.

The patient was wholly unable to use his left hand. Yet when he was given a book to hold in the left hand, he would hold it upside down and make fruitless attempts to open it and turn the pages, but never was able to do so. All the while he would say, "I can do this, just give me time." When the examiner informed him that something seemed to be wrong with his left hand, he denied any difficulty, saying, "There must be something wrong with the book."

The patient was able to walk only by holding on to a table, and then with the greatest difficulty. He would walk headlong into a wall or a chair. When trying to walk, having great difficulty, he would say, "Just let me alone. I can walk. If my glasses were only right."

The three defects—blindness, inability to use the left upper extremity, and inability to walk —were all vigorously denied. When an examiner insisted that one of these defects was present, the patient showed flushing of the face, increase in seemingly purposeless movement, tearing of the eyes, and persistent denial of dysfunction.

Occasionally, when asked why he was in the hospital, the patient would say, "My eyes are bothering me." On closer questioning, he would say that his vision was good but that there was "something the matter with my glasses."

Laboratory Examinations.—The results of a complete blood count, urinalysis, serologic tests, and blood urea nitrogen, creatinine, and cholesterol determinations were all normal. Examination of the spinal fluid revealed normal constituents. Electrocardiographic tracings showed changes compatible with an old myocardial infarction of the posterior wall. The electroencephalographic record was grossly abnormal, showing "an extensive slow-wave defect in the entire right hemisphere, with waves of 2 to 5 per second frequency. Opening and closing of the eyes demonstrated slight lowering of amplitude. The record was thought to be compatible with a vascular lesion or lesions." A roentgenogram of the chest and skull were within normal limits except for mild emphysema. Repeated blood cultures yielded no growth. Psychometric examination was done soon after admission. At this time the patient was unable to see. The intelligence quotient was 101. Verbal facility, the fund of general knowledge, and vocabulary were excellent. There was some defect in concentration and attention. The patient did poorly on arithmetical problems and comprehension of proverbs. Some defects in remote memory were found. In summary, it was stated that "the present functioning of the patient shows marked variability. The impairment of abstract ability, memory loss, and difficulty with tasks requiring concentration and attention are characteristically associated with structural brain damage."

Hospital Course.—The patient's condition did not change during the first two weeks in the hospital. Therapy with nicotinic acid and papaverine was instituted.

During the next 10 weeks in the hospital, the patient gradually improved. He became able to walk without difficulty. His vision improved, and he was able to recognize people and objects. The motor power in the left arm improved also. As he improved, he gradually stopped denying his defects. The first evidence of this occurred when, in the 5th week of hospitalization, he admitted to his wife in confidence that "he couldn't see very well." In his 12th week, he

admitted to his physician that his vision was a "little blurred" but was "getting better." He stated that his arm was a "little weak." He described his gait as "normal," as in fact it was.

Sodium-Amobarbital Interview.—Later in the patient's hospital course, when he admitted that he saw poorly and that his left upper extremity was weak, small doses of amobarbital sodium were administered intravenously. This caused him to readopt the previous attitude of denial of blindness and weakness of the arm. At such times he was disoriented and easily roused to confabulation. These changes disappeared as soon as the amobarbital effect cleared.

The patient was considered to have, "vascular disease of the brain, diffuse," and possibly "multiple cerebral emboli, from a mural thrombus secondary to myocardial infarction, old."

Experimental Observations.—To determine the manner in which a patient with a denial syndrome reacts to a mechanically induced motor defect in a nondiseased extremity, we made the following observations on our two patients:

PATIENT 1.—On the fourth day of her hospitalization the patient described her left arm as "sick"—"He's sick." At this time there were defects in motor ability and coordination in the left arm, as have been described. When questioned about her right hand, which showed no neurological defects, she stated," "It's all right; there's nothing the matter with it." She demonstrated that she could turn the pages of a magazine with her right hand.

At this point, the patient's eyes were covered as she rested in bed. Her right arm and hand were immobilized by means of a wooden arm board and heavy bandages. Upon being asked to turn the pages of the magazine with her right hand, she was unable to do so and appeared anxious and continually attempted to manipulate the pages. When asked about her obvious difficulty with the right arm, she said, "My arm—he feels funny—he's sick, sick again," indicating her right arm. When asked whose arm she was referring to, she replied, "It's his arm, not mine—he's sick," again pointing to her right arm.

When the arm board was removed from the right arm and her eyes were uncovered, she appeared relieved. A few minutes later, she was able to turn the pages of the magazine with the right arm without anxiety or comment.

PATIENT 2.—On the patient's second and third days in the hospital, he was persistently denying his visual loss, difficulty in walking, and his inability to use his left arm. When asked if he could see, he replied in the affirmative and incorrectly described objects placed before him. When asked to turn the pages of a book with his left hand (the side with pronounced motor and sensory defect), he stated, while making futile attempts to do so, "I can do it; my arm is OK; just give me some time. . . . There must be something the matter with this book." He was able to turn the pages of the book with his intact right hand. When asked about his right hand, he said, "It's fine—there; I can turn them fine."

At this point, the patient's right arm and hand (his intact extremity) were bound to a wooden arm board with heavy bandages, completely immobilizing them. Because he was blind, no covering of the eyes was necessary. When asked to turn the book pages with his immobilized right hand, the patient was unable to do so, although making persistent attempts. When asked why he was having this difficulty, he said, "I can do it; just give me time." When asked if there was anything wrong with his right hand, he replied, "No, it's all right; I could turn those pages if I had the proper glasses." After attempting to use the bound right hand for 15 minutes, still denying inability to use it, he said quietly, "Maybe there is something tied to my arm." The patient seemed agitated and anxious during this period. When the arm board was removed, he was able to turn the book pages with his right hand, saying proudly, "There, I can do it fine."

These experimental data indicate that the patient with a denial syndrome will impose his particular attitude of denial upon experimentally induced defects in an intact extremity.

COMMENT

Anosognosia means literally, "Without knowledge of disease" (*a*, without; *noso* disease; *gnosia*, knowledge). It has variously been used to describe denial of a dysfunction (i. e., hemiplegia), denial that an affected organ is a part of the individual's body, and denial of the existence of a part of the body even when there is no gross structural defect which impairs its function. In the two cases which

we have described, the experiments with the arm board have also demonstrated the denial of dysfunction in a nondiseased part, thereby extending the possibilities. In Weinstein's concept, the term also embraces denial of events in the patient's recent experience, such as illness, operation, and incontinence.[4] While such extensions of the definition may be justified by the etymology of the word "anosognosia," it should be recognized that these broader concepts are far from the original meaning of the term as employed by Babinski to denote denial of the left hemiplegia.[5]

The one characteristic which is common to all these clinical situations is best described as an attitude of denial in the face of threatening reality. The pattern of denial as recounted in the literature, because of its associations with so great a variety of anatomical lesions, defies topographical localization. Anosognosia in patients with brain tumors in sites other than the classic location (interruption of thalamoparietal pathways in the minor hemisphere) has been demonstrated by Weinstein and associates and other authors.[4] Psychogenically determined difficulties with body parts, including denial, have been seen in hysterical persons and produced by hypnotic suggestion (Teitelbaum[6]). In this regard, as a function of human emotional experience, it may be recognized in the same category as other defense mechanisms, such as repression. In our patients the syndrome may be conceived of as an adaptation to stress found in persons who are facing internal disorganization and an inability to cope with the demands of the environment.

This defense—the attitude of denial—is seen most clearly, as others before us have pointed out, against a background of disorientation, poor contact with the environment, and confabulation.[4] However, as both our cases indicate, the proclivity for denial is not a temporary defense adopted by a patient with gross structural brain disease to protect himself against the threat of a particular situation. It is doubtful whether cortical atrophy or vascular disease of the brain and denial of defects or body parts have any particular relationship to each other. The attitude of denial of illness is probably a lifelong pattern. When employed to face some minor illness, such as an upper respiratory infection or a small burn, denial excites no comment. However, when set against a background of disorientation, confusion, and confabulation, and when used to meet the dramatic threat of hemiplegia or blindness, the denial attitude stands out. At such a time this behavior is so bizarre as to make it worthy of note in the medical annals. Our second patient, because of childhood preoccupation with illness and because he feared illness all his life, always denied the presence of major illnesses in others (including his wife) and himself. When blindness, paralysis, and intellectual defect supervened, he denied all illness except a trifling defect in his eyes. With reassurance this attitude became less pronounced, only to reappear when amobarbital-induced disorganization made it apparent once more.

The personal history in Case 1 revealed a woman with immature behavior and with excessive lifelong preoccupation with handedness, twinning, and dichotomies of good and evil. Her associations of "left" and "bad" and "him" have been

5. Babinski, J.: Contribution à l'étude des troubles mentaux dans l'hemisplégie organique cérébrale [anosognosis], Rev. neurol. **22**:845-848, 1914.

6. Teitelbaum, H.: Psychogenic Body Image Disturbances Associated with Psychogenic Aphasia and Agnosia, J. Nerv. & Ment. Dis. **93**:581-612 (May) 1941.

referred to in the protocol. There was strong evidence that she had faced threatening life situations in the past with left-sided denial. With psychotherapy (suggestion, reassurance) her attitude underwent sufficient change to free her of most of her defects. The return of the denial syndrome following pneumoencephalogram and the injection of amobarbital sodium can be understood in terms of her previously demonstrated response to life stresses, both internal and external. Even a transitory urinary incontinence was denied at this time.

In keeping with their habitual patterns of reaction, both patients reacted to the experimental production of dysfunction in the arm-board test. The controlled production of the gross motor defect in an intact extremity was dealt with by further denial of dysfunction, this time in the unaffected extremities. Of course, only a person with poor contact with the environment can be expected to ignore the very real limitations of motion created by the board; but it is interesting to note that in referring to the new loss both patients used the same descriptions as they were applying to their presenting complaints.

SUMMARY

Two cases of a denial syndrome, heretofore referred to as "anosognosia," are described in detail. It has been shown that the denial syndromes were related to the premorbid personalities of these two patients. A specially devised "armboard test" is described which lends support to the above thesis and casts further doubt on the theory that anosognosia is a topographically determined symptom of lesions interrupting the thalamocortical pathways of the minor cerebral hemisphere.

DESOXYCORTICOSTERONE THERAPY IN CERTAIN PSYCHOTIC CASES

An Interval Report

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DESOXYCORTICOSTERONE acetate,[1] a synthetic steroid, has been used as therapy, since 1948, for psychotic patients in a program of evaluation of its effect on the psychoses. A preliminary report was published in 1949.[2] The present report concerns the latest results of the study, namely, the recorded observations from August, 1949, to April, 1951.

The project was undertaken on the basis of an assumption that patients with psychoses are subjected to repeated and overwhelming stress, which results in depletion. In this situation desoxycorticosterone acetate would supply a replacement therapy. This concept has been strengthened and enlarged by several publications, especially that by Hoagland and associates,[3] who have proposed that convulsive shock therapy acts theoretically by causing a release of endogenously produced corticotropin. Reiss and associates [4] have shown that certain psychotic patients who did not show an adrenocortical response to a test dose of corticotropin showed no improvement after convulsive shock therapy.

METHOD

Twenty-one subjects were selected from the group of psychotic patients who failed to respond favorably to electric shock, or insulin, or both, and psychotherapy. For the most part, the patients selected for treatment with the steroid were hyperactive, and many were aggressive as well.

Each patient was matched with a control patient. The control subject, so far as was possible, resembled the patient in diagnosis, degree of aberration, age, sex, duration of illness, and length of hospitalization.

Prior to the beginning of treatment, records were made of weight, blood pressure, urinary constituents, blood serum chloride and cholesterol, and circulating eosinophiles. Three eosinophile determinations were made, at weekly intervals.

The patients and the controls were followed closely with the same laboratory tests and method of clinical evaluation. On specified days the patients and controls were interviewed. Findings were also recorded by an observer other than the examiner several times a week.

The treatment consisted of intramuscular injections of 5 mg. of desoxycorticosterone acetate daily, six days a week. Since the steroid was administered in 1 cc. of sesame oil, the controls were given 1 cc. of sterile sesame oil intramuscularly at the same intervals. This treatment pattern remained standard until a result, either sustained clinical improvement or failure, was established.

From the University of Oregon Medical School.

1. The desoxycorticosterone acetate used was doca® acetate, of Organon, Inc.

2. Jens, R.: Northwest Med. **48**:609, 1949.

3. Hoagland, H.; Calloway, E.; Elmadjian, F., and Pincus, G.: Psychosom. Med. **12**:73, 1950.

4. Reiss, M.; Hemphill, R. E.; Maggs, R., and Haigh, C. P.: Brit. M. J. **2**:634, 1951.

When clinical improvement appeared to be sustained, the dose was reduced to 5 mg., given four times a week. As improvement was maintained, the dosage was reduced to 5 mg. twice a week. In the event of failure to improve, the patient and the control were simultaneously dropped from the treatment program.

EVIDENCE OF TOXICITY

Three years of clinical application of the drug has brought out some interesting facts. There have been no casualties or serious ill-effects. No evidence has appeared to date to indicate that any lasting deleterious result has occurred from this therapy.

An undesired effect was edema of the ankles. One patient had edema of both ankles. The edema disappeared when the steroid was discontinued. The elevation of blood pressure was fairly consistent throughout treatment, with an average of 24 mm. systolic and 11 mm. diastolic; the pressures returned to pre-treatment values on discontinuation of medication. In summary, it may be stated that no unpleasant symptoms were complained of during treatment. Signs were limited to moderate elevation of blood pressure and, in one case, to edema of the ankles.

COMMENT

The desirability of establishing objective criteria for evaluation of the effectiveness of desoxycorticosterone therapy was apparent from the very beginning of the study. The difficulty in obtaining such data became increasingly apparent as one index after another was adopted, only later to be rejected.

Blood serum chloride and cholesterol values were determined at regular intervals during a two-year period. Variability in the values obtained finally led to their abandonment as a treatment index.

Circulating eosinophiles were counted within half an hour after injections of desoxycorticosterone or sterile sesame oil. A zero value was frequently, but not consistently, present at this interval after injection of desoxycorticosterone. On the other hand, a zero value not infrequently was obtained in control patients, who received simply sterile sesame oil.

RESULTS

The criteria for judging the results were set as follows:

Patients who were allowed to go home (returned home) assumed the responsibilities they had carried prior to hospitalization. These patients were judged to show complete remission of their disease.

Patients who were able to work in the industrial departments of the hospital were considered unqualifiedly improved. Industrial-department requirements are such that patients must have considerable initiative and be able to work with a minimum of supervision and with negligible direction.

Patients who improved to the extent that they helped with ward routine were considered moderately improved. Patients who work in the ward have preliminary and, if necessary, repeated instruction and regular supervision.

Patients who did not fit into any of the three preceding categories were judged unimproved.

In Table 1 are listed, in protocol form, the results obtained.

Four patients have gone home. One woman will be permitted to leave as soon as the details in connection with her employment can be worked out. The details of her case are given as an example.

TABLE 1.—*Results of Treatment*

Case No.	Age, Yr.	Diagnosis	Date of Onset	Other Treatment	Desoxycorticosterone Acetate, 5 Mg. Doses, Wk. of Therapy	Result
1	31	Manic-depressive psychosis, manic	Recurrent since 1933	4 EST*; full restraint	6	Returned home 6/6/49
2	21	Schizophrenia, catatonic type	Recurrent since 1944	43 EST; insulin full restraint	27	Returned home 12/23/49
3	40	Psychosis with mental deficiency	1948	9 EST	34	Returned home 1/6/50
4	37	Schizophrenia, mixed type	1949	.....	10	Returned home 3/3/50
5	23	Schizophrenia, catatonic type	1949	14 EST	14	Improved
6	35	Manic-depressive psychosis, manic	1921	17 EST; insulin	9	Improved
7	59	Schizophrenia, paranoid type	1949	3 EST	18	Improved
8	34	Schizophrenia, paranoid type	1948	18 EST; insulin	52	Improved
9	36	Manic-depressive psychosis, mixed type	1945	24 EST; insulin	23	Improved
10	55	Involutional psychosis, paranoid type	1946	62 EST	22	Improved
11	36	Manic-depressive psychosis, manic phase	1945	40 EST; lobotomy (5/27/50)	26	Moderately improved
12	33	Schizophrenia, mixed type	1947	22 EST; full restraint	63	Moderately improved
13	31	Manic-depressive psychosis, manic phase	1945	23 EST	37	Moderately improved
14	51	Involutional psychosis, melancholia	1944	96 EST	38	Moderately improved
15	20	Schizophrenia, unclassified	1948	21 EST	44	Moderately improved
16	46	Manic-depressive psychosis, manic phase	1944	.....	65	Moderately improved
17	33	Schizophrenia, catatonic type	1949	28 EST; insulin	14	Moderately improved Treatment terminated—patient returned to state of residence
18	26	Schizophrenia, catatonic type	1947	7 EST	25	Failure
19	60	Manic-depressive psychosis, manic phase	1949	55 EST	40	Failure
20	28	Schizophrenia, mixed type	1946	12 EST Full restraint	27	Failure
21	24	Schizophrenia, hebephrenic type	1948	3 EST Also combined insulin and EST	34	Failure

* EST stands for electric shock therapy.

A woman aged 23 had been ill for almost two years with a condition diagnosed as schizophrenia, catatonic type. Except for relatively short intervals, she retained ability to record her subjective sensations throughout the course of treatment. Excerpts from her daily diary follow:

Jan. 12, 1951 (After two weeks on daily injections of desoxycorticosterone [5]) "I seem to have dreamy streaks, Doctor. Maybe it's my thyroid or something. Hope Doca [5] clears it up."

Jan. 14: "I still think sometimes that I'm being watched or that people of importance around the hospital, like the student nurses, can hear what I say when they're not around. I don't have this attitude all of the time. I know they can't, but it's just a feeling. Suspicion is a sign of insanity, I've been told. Perhaps I've been misinformed. I hope that I get over this attitude of imagining people can hear what I say."

Jan. 17: "I have flashes of light in front of my eyes—I'd say approximately five or six times a day, and some days not any. I've had this condition off and on for over a year. Others say they can't notice any light when I do; so guess it's just my condition."

8 p. m. (same day): "Others say they can see the flashes and it must be electric lights; so I'm not as screwy as I thought I was."

Jan. 20: "I'm just fine this morning, no funny ideas, no voices."

Feb. 1: "Am feeling fine. No peculiar ideas."

Feb. 3: "I'm still grateful for being mentally competent again."

Six patients are employed in the industrial department of the hospital.

TABLE 2.—*Results of Studies Showing Improvement Following Desoxycorticosterone Therapy* *

	Present Study		Early Study		Combined Studies	
	DCA	Controls	DCA	Controls	DCA	Controls
Total no. of patients treated.....	21	26	16	16	37	42
No change	4	19	4	15	8	34
Improvement	14	5	8	0	22	5
Recovery	3	2	4	1	7	3

* The chi-square test for association indicated that such a difference between the two groups has a possibility of less than 1 in 100 of arising from errors in sampling.

One woman of this group, aged 55, with a diagnosis of involutional psychosis, paranoid type, at the time of admission and for a long time thereafter, required tube feeding and had to be assisted with all the details of her personal needs.

Almost a month after treatment with desoxycorticosterone had been started, her case was reevaluated; at that time she was observed to have dark, almost bronzed skin. A Kepler-Fowler test yielded results not incompatible with true Addison's disease.

She was treated with desoxycorticosterone for 22 weeks. Twenty months after the last injection of desoxycorticosterone acetate, she was working in the laundry, where she had worked regularly for nine months. This patient should return home soon if the family's resistance can be overcome. The family's resistance is based on her prehospitalization behavior and is understandable in the light of their experience with the patient.

Seven patients have shown moderate improvement. Four showed no improvement, and the treatment of these four patients was judged a failure.

Results in the group of patients used as controls were very different from those in the treatment group. Only one subject returned home. Three patients improved sufficiently to work in the industrial department of the hospital, and one of these three patients has maintained improvement long enough that his return home can be anticipated. One showed moderate improvement; the rest are not improved.

The tabulated results are shown in Table 2.

5. All patients refer to their treatment as Doca.® Control patients are unaware of the difference in the injection ingredient.

SUMMARY AND CONCLUSIONS

Desoxycorticosterone acetate in sesame oil was administered to 21 psychotic patients; sesame oil in the same amounts without the steroid was administered simultaneously to controls.

Patients employed in this study had not responded with improvement to earlier therapy with electric shock, or insulin, or both, and psychotherapy.

Twenty-one patients were selected, all of whom were difficult to manage; their disorders were classified as manic-depressive psychoses, schizophrenia (all types), involutional psychoses, and psychoses associated with mental deficiency.

The results of treatment with the steroid were as follows: Four patients were sent home, having had a remission of disease; a fifth is being prepared for employment; six are employed in the industrial departments of the hospital; seven assist with duties in connection with ward routine. Four (19%) are unimproved. In all, 17 (81%) are improved.

Sustained improvement occurred after from six to eight weeks of the desoxycorticosterone therapy.

Patients who served as controls presented very different results; i. e., only 1 returned home, having had a remission of the psychosis; 4 showed improvement; 2 showed moderate improvement; 19 (73%) were unimproved.[6] In all, 7 (27%) remained improved.

The results of this study are in agreement with the results we reported earlier.[2] Larger-scale evaluation of therapy with desoxycorticosterone acetate is indicated.

Dr. Carl E. Hopkins, of the University of Oregon Medical School, assisted in the statistical analysis.

6. There were 26 control patients, as against 21 patients on regular treatment, since hospital management made it necessary to replace control patients on occasion and the results for all patients are listed.

DISTURBANCES OF VIBRATORY SENSE (PALLESTHESIA) ASSOCIATED WITH NERVE ROOT COMPRESSION DUE TO HERNIATED NUCLEUS PULPOSUS

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IN THE extensive literature concerning intervertebral-disk derangements there has been little comment on vibratory sensation (pallesthesia). This is understandable, since examination of motor power, reflexes, and the sensory modalities of pain and light touch, together with myelography, may make further neurological testing seem superfluous. However, vibratory perception may be impaired or lost in certain localized areas in patients with these lesions, and this paper is a report of 16 such cases. In 14 cases the location of the lesion was proved by myelography and operation, and in 2 cases, by myelography alone. In two of the cases tests were made with a vibrometer [1] in addition to the usual methods, so that quantitative comparisons of vibratory perception were possible. In both instances the findings with the vibrometer were similar to the results with a simple tuning fork (C 128).

Disturbances in pallesthesia were not found in all cases of motor and sensory disturbances due to herniated nucleus pulposus, being present in about 20 to 30%.

FIRST SACRAL NERVE ROOT (FIFTH LUMBAR-FIRST SACRAL DISK)

This group comprised eight cases, the disturbance being on the left side in four cases and on the right side in four cases. All the lesions were verified at operation. The Achilles reflex was absent on the involved side in five cases, depressed in two cases, and absent bilaterally in one case.

In one case there was weakness of the "hamstring," peroneal, gluteal, and anterior tibial muscles. Myelography demonstrated a complete subarachnoid block at the level of the fifth lumbar interspace. At operation a large protrusion of the nucleus pulposus was found at this level, with severe compression of the first sacral nerve roots, especially on the side of the weakness and sensory changes. No motor weakness was present in the other seven cases.

In seven cases areas of hypalgesia and hypesthesia on the lower extremity corresponded closely to the distribution of the first sacral nerve root, as described by Keegan.[2] No hypesthesia or hypalgesia was demonstrable in the eighth case, in which, however, there was decreased vibratory perception over the fifth toe, the fifth metatarsal, and the medial malleolus.

From the Neurological Surgery Service, Franklin Hospital, and the Department of Neurological Surgery, University of California Hospital.

1. Collens, W. S.; Zilinsky, J. D., and Boas, L. C.: Clinical Vibrometer: An Apparatus to Measure Vibratory Sense Quantitatively, Am. J. Med. **1**:636-637 (Dec.) 1946.

2. Keegan, J. J.: Dermatome Hypalgesia Associated with Herniation of Intervertebral Disk, Arch. Neurol. & Psychiat. **50**:67-83 (July) 1943.

In two cases there was pallanesthesia of the small toe, with pallhypesthesia of the other toes and the fourth and fifth metatarsals. In a third case there was pallanesthesia of the fourth and fifth toes, with pallhypesthesia of the other toes, the foot, both malleoli, the tibia and the patella (slight).

In the remaining five cases vibration was decreased in the following locations: fifth toe, all five cases; fourth toe, three cases; third toe, two cases; second toe, one case; fourth and fifth metatarsals, two cases; entire foot (greater loss laterally), two cases, and lateral malleolus, two cases.

FIFTH LUMBAR NERVE ROOT (FOURTH-FIFTH LUMBAR DISKS)

Eight cases comprised this group, six with lesions on the left side and two with lesions on the right side. In six cases myelography was followed by operation; in two cases myelography, by conservative treatment.

Zones for pallesthesia for the fifth lumbar and first sacral nerve roots. The solid area shows a relatively autonomous distribution; the hatched areas, overlapping distribution.

In seven cases there were varying degrees of weakness of the anterior tibial muscle group. Tendon reflexes were normal in six cases. The Achilles reflex was slightly depressed in one case, and both the Achilles and the patellar reflex on the side of the lesion were slightly depressed in the other.

In seven cases hypalgesia and hypesthesia occurred in the area of the fifth lumbar nerve root, in a distribution similar to Keegan's description [2] except that the hallux was usually involved and the sensory loss above the knee was vague and difficult to outline. In the eighth case a small area of hypalgesia was noted on the dorsum of the foot.

In two cases there were areas of pallanesthesia. In one case vibratory perception was absent in the second, third, and fourth toes and diminished in the first toe and foot (greater loss mesially). In the other case there were pallanesthesia of the first, second, and third toes and pallhypesthesia of the first metatarsal, the medial malleolus, and the tibia.

In the remaining six cases there was pallhypesthesia of the following areas: hallux, three cases; second toe, four cases; third toe, four cases; fourth toe, three cases; small toe, two cases; first and second metatarsals, two cases; all metatarsals, three cases; medial malleolus, two cases; lateral malleolus, one case, and tibia, two cases.

COMMENT

It appears from this limited study that the zones of nerve-root distribution with respect to pallesthesia resemble the corresponding zones for pain and light touch sensibility, at least in the domain of the fifth lumbar and first sacral roots. Because of the nature of the stimulus and its transmission by bone, determination of pall-anesthesia and pallhypesthesia is more difficult than that of analgesia or anesthesia when confined to a small area, but it can be done with careful testing and cooperation of the patient. The vibrometer may be helpful.

The zones of pallesthesia show a moderate degree of overlap but are more autonomous in the distal than the proximal part of the extremity. The zone of the fifth lumbar nerve root (Figure) appears to include the second and third toes, with overlap onto the first and fourth toes, the metatarsals (mainly first, second, and third), and the lower portion of the tibia. The zone of the first sacral nerve root (Figure) includes the fourth and fifth toes with overlap onto the second and third toes, the metatarsals (mainly fourth and fifth), and the lateral malleolus. It can be seen that these zones resemble previously described dermatomes fairly closely.

No disturbances in position sense were demonstrable in these cases. Perhaps a quantitative method of testing would reveal some defect in this modality.

SUMMARY

Disturbances in vibratory perception (pallesthesia) in 16 cases of compression of single nerve roots by a herniated nucleus pulposus are described, and the zones of distribution, with respect to pallesthesia; of the fifth lumbar and first sacral nerve roots are outlined. In one case there was impairment of pallesthesia without impairment of the other sensory modalities tested.

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Dr. Howard A. Brown, Dr. O. W. Jones, and Dr. Eugene M. Webb permitted me to examine the patients on whom this report is based.

DENIAL OF ILLNESS

Its Occurrence in One Hundred Consecutive Cases of Hemiplegia

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MANY DESCRIPTIONS of the phenomenon of denial of illness have been published.[1] The literature contains little, however, concerning the frequency of its occurrence. The purpose of this investigation was to determine the incidence of denial of illness in patients with hemiplegia. We chose hemiplegia because of its prevalence and extensive somatic involvement and for historical reasons. The study also permitted us to observe denial of illness in relation to the mental state of the patient, the side of the body involved, and other factors.

The term anosognosia, introduced by Babinski in 1914,[1e] referred to two cases of left hemiplegia, but it has subsequently been used by others to denote denial of other illnesses as well. Another phenomenon, the denial of existence of a part of the body, sometimes called autotopagnosia or somatoagnosia,[1g] has at times been

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1. (*a*) Weinstein, E. A., and Kahn, R. L.: The Syndrome of Anosognosia, Arch. Neurol. & Psychiat. **64**:772-791, 1950. (*b*) Henson, R. A.: On Thalamic Dysesthesiae and Their Suppression by Bilateral Stimulation, Brain **72**:576-598, 1949. (*c*) Head, H., and Holmes, G.: Sensory Disturbances from Cerebral Lesions, ibid. **34**:102, 1911. (*d*) Hemphill, R. E., and Klein, R.: Contribution to the Dressing Disability as a Focal Sign and to the Imperception Phenomena, J. Ment. Sc. **94**:611, 1948. (*e*) Babinski, J.: Contribution à l'étude des troubles mentaux dans l'hémiplégie organique cérébrale (anosognosie), Rev. neurol. **22**:845-848, 1914. (*f*) Barkman, A.: De l'anosognosie dans l'hémiplégie cérébrale: contribution clinique à l'étude de ce symptome, Acta med. scandinav. **62**:235, 1925. (*g*) Alajouanine, T.; Thurel, R., and Ombredane, A.: Somato-agnosie et apraxie du membre supérieure gauche, Rev. neurol. **41**:695, 1934. (*h*) Egas Moniz; Almeida Lima, and de Lacerda, R.: Hémiplégies par thrombose de la carotide interne, Presse méd. **45**:977, 1937. (*i*) Nielsen, J. M.: Gerstmann Syndrome: Finger Agnosia, Agraphia, Confusion of Right and Left and Acalculia, Arch. Neurol. & Psychiat. **39**:536, 1938. (*j*) Nielsen, J. M., and Sult, C. W.: Agnosias and the Body Scheme, Bull. Los Angeles Neurol. Soc. **4**:69, 1939. (*k*) Olsen, C. W., and Ruby, C.: Anosognosia and Autotopagnosia, Arch. Neurol. & Psychiat. **46**:340, 1941. (*l*) Spillane, J. D.: Disturbances of the Body Scheme: Anosognosia and Finger Agnosia, Lancet **1**:42, 1942. (*m*) Gerstmann, J.: Problem of Imperception of Disease and of Impaired Body Territories with Organic Lesions, Arch. Neurol. & Psychiat. **48**:890, 1942. (*n*) Sandifer, P. H.: Anosognosia and Disorders of Body Scheme, Brain **69**:122, 1946. (*o*) Schilder, P.: The Image and Appearance of the Human Body: Studies in the Constructive Energies of the Psyche, Psyche Monographs No. 4, Kegan Paul, Trench, Trubner & Company, Ltd., 1935. (*p*) Weber, F. P.: Agnosia of Hemiplegia and of Blindness After Cerebral Embolism, Lancet **1**:44, 1942. (*q*) Roth, M.: Disorders of the Body Image Caused by Lesions of the Right Parietal Lobe, Brain **72**:89-111, 1949.

confused with anosognosia. For the sake of clarity, we decided to abandon both these terms and refer to the phenomenon simply as denial of illness. We considered that a patient with a completely paralyzed extremity who maintained (1) that he could move the involved limb, (2) that it was not paralyzed or weak, or (3) that there was "nothing wrong" with it had denial of hemiplegia. In this report, although the terms "lack of awareness" and "denial" are often used interchangeably, they actually may have different implications, a point which will be discussed later.

MATERIAL AND METHOD

One hundred consecutive patients with hemiplegia were interviewed in Bellevue Hospital Center (Third and Fourth Divisions, Medicine, Neurology and Psychiatry). All were asked the same questions and given the same commands from a prepared form, which is reproduced here. The answers to the questions were recorded exactly as offered by the patient, and detailed descriptions of their responses to these commands were made. The ages ranged from 29 to 86 years, with an average age of 61.

Part 1.

1. Why are you here?
2. What is the matter with you?
3. Is there anything wrong with it (part involved)?
4. Is there anything wrong with it? (Examiner either points to or raises it.)
5. Can you move it? Raise it? etc.
6. Is it weak, paralyzed, numb? How does it feel?
7. What is this? (Examiner holds up part involved and shows it to patient.)

Part 2.

The questions concern orientation in time and space, ability to understand commands, general information, and attempts to elicit confabulation ("Have you ever seen me before?"; "Where were you last night?")

The questionnaire consisted of two parts. Part 1 was aimed at determining the patient's awareness of his illness, and Part 2, at determining his orientation and ability to understand and carry out commands. The questions were simple and direct and varied in wording, in order that cultural and educational differences should be eliminated. The interview began with general questions, such as, "Why are you in the hospital?" "Are you sick?," etc., and proceeded to more specific questions, such as, "Anything wrong with your arm?" "Anything wrong with it?" (examiner touching and lifting the involved part), and, "Can you move it?" This part was followed by questions to elicit evidence of an organic mental syndrome.

The same series of questions and commands was given to all patients with aphasia except those whose speech disorder was so severe that no contact could be made.

In this report, the term hemiplegia is used to mean complete paralysis of one or both extremities on one side of the body. When movement was present to the extent that the arm could be raised,[2] the case was not included. Patients with less severe abnormalities also may have denial of illness, but in order that the significance of responses to specific questions, such as "Can you move your hand?," should be interpreted more accurately, the criterion of complete paralysis was necessary.

The clinical diagnosis in more than 95% of this series was cerebrovascular accident, either intracerebral hemorrhage or occlusion of a major cerebral vessel. The remaining five patients had cerebral neoplasm (one primary and one metastatic), syphilis of the nervous system, and traumatic encephalopathy.

RESULTS

Patients with Denial of Illness (Group 1).—Of the entire series of 100 patients with hemiplegia, 28 had denial of illness. This included five patients who, although they sometimes gave evidence of awareness of their illness, for the most part denied their defects. For example, two of the patients admitted that they had had a

2. Since we did not encounter any patients whose lower extremity was paralyzed and the upper relatively spared, the questions were referred mainly to the upper extremity.

"stroke" but insisted that they could move or walk. The others fluctuated in their responses from awareness to total denial. Twenty-three patients of this group unequivocally and consistently denied that they were ill, denied that their extremities were weak or paralyzed, and claimed that they could move them.

Patients with Full Awareness of Illness (Group 2).—Forty-eight patients were able to indicate clearly and promptly the nature and extent of their illness. They were aware of their paralysis and of the reasons for hospitalization and readily admitted the extent of their disability. As will be shown later, this awareness was not always complete, and, on being further questioned, several patients gave hints of minimizing or ignoring their defects.

Patients with Whom No Verbal Contact Could be Made (Group 3).—This group consisted of the remaining 24 patients, who presented right hemiplegia and severe aphasia.

ANALYSIS OF FACTORS IN DENIAL

In the groups in which denial of illness was unequivocally present (Group 1) or absent (Group 2), analysis of the following factors was made: (1) presence of organic mental syndrome; (2) side of the body involved and, if the dominant side was involved, presence of aphasia, and (3) length of time the hemiplegia had been present.

Mental Status.—In Group 1 (with denial of illness) all the patients showed some degree of disorientation. The spheres of orientation most involved were time and place. Memory defects were less apparent, possibly because the patients' responses were more difficult to verify. This finding contrasts strikingly with that in Group 2, (patients who did not deny illness). In this group only 31% (15 of 48 patients) had an organic mental syndrome, whereas 56% (27 of 48 patients) did not have this defect, by the criteria described. In 12% (6) of the patients it was difficult to determine whether or not an organic mental syndrome was present, although they readily indicated awareness of their illness. Almost one-third (8 of 28) of the patients with denial of illness were in the psychiatric wards, whereas of those who did not deny illness, only one-ninth (5 of 48) came from the psychiatric pavilion.

Patients on whom repeated observations could be made presented denial of illness in direct relation to their degree of disorientation. The patient who denied his hemiplegia when grossly disoriented often admitted the defect when more alert and better oriented. In a series of 58 consecutive disoriented patients examined by Weinstein,[3] 52 had denial of illness.

Side of Involvement.—A comparison of the groups showed a striking difference in regard to the side of the body involved. (Since there was only one patient with left hemiplegia and aphasia in the entire series, the term "dominant side" will not be used in this discussion.) Of the 28 patients who denied illness, 19 (69%) had left hemiplegia; 6 (21%) had right hemiplegia with aphasia, and 3 (11%) had right hemiplegia without aphasia. Of the 48 patients without denial of illness, 18 had left hemiplegia, 17 had right hemiplegia with aphasia, and 13 had right hemiplegia without aphasia.

3. Weinstein, E. A.: Personal communication to the authors.

Presence of Aphasia.—The problem arose of classifying the patients with severe aphasia, who had to be included in an unselected series. The distribution of right and left hemiplegia in the two groups may be artificial because there is no way of knowing whether the patients with global aphasia denied their defects or not. There is no satisfactory way of evaluating the severely aphasic group, but it is reasonable to assume that some of them had denial of illness.

It is evident that the presence of aphasia is not incompatible with denial of illness. While a reliable evaluation of denial of illness is usually impossible in patients who have a predominantly receptive aphasia, such an evaluation can be made in most patients with motor aphasia. All the aphasic patients (24) with whom adequate communication could be established had expressive aphasia. Seventeen of these 24 patients fully realized and indicated the extent of their defects, and 7 gave equally convincing evidence of denial of illness.

Time Factor.—In all the groups the hemiplegia had existed for periods ranging from one day to several years. There were representatives from each of the three groups in all periods in time. The individual numbers, unfortunately, were too small for statistical evaluation.

The factor of age proved not to be significant in this study, since the average age of the patients with denial of illness was 60, as compared with 62 for those who were aware of their illness.

Other Factors Observed in Patients with Denial of Illness.—The nature and character of the remarks made by the patients with denial of illness, either spontaneously or in response to various questions, suggest some of the underlying mental processes involved in this phenomenon.

Several of the explanations offered for their present situation involved other persons, usually members of their own families or the physician—for example, "My brother told me my hand was paralyzed," or "Well, that's what I was told by the doctors; I suppose the doctors know what they say." One patient, when asked whether he was paralyzed, said, "I have no way of determining that; I'm not a physician." Another, when asked whether her right hand was paralyzed, said, "Well, the doctors say it is; so I guess it is," or, "I was told it was weak."

Rationalizations were common and often grossly unrealistic. One patient, when asked why she could not move her hand, said, "Somebody has a hold of it." Another patient, asked if anything was wrong with her hand, said, "I think it's the weather; I could warm it up, and it would be all right." One woman when asked whether she could walk said, "I could walk at home, but not here. It's slippery here." One patient, when asked if anything was wrong with his arm, said, "It's just a little stiff—from the cold or something." When asked why he couldn't raise it, he said, "I have a shirt on." A common explanation was "stiff joints," one which could have been accepted if the same patients had not claimed that they could move their paralyzed extremities.

Another said she entered the hospital "because I lost a lot of weight." Others gave a variety of unrelated somatic complaints.

Patients occasionally used facetious expressions, such as, "I came here to see you," when they were asked to explain their coming to the hospital. One woman who was almost moribund, dyspneic, and cyanotic stated, "I came for a vacation." Another said, "I guess New York State has a lot of money to waste."

Others were hostile throughout the examination and made statements like, "If I weren't sick I wouldn't be here, would I?"

Some of the responses given by the patients were frank confabulations. One patient claimed she was "here at home last night." Another said she was in church last night. Others stated that they knew the examiner from previous contacts.

Denial of Existence of Affected Extremity: Several of the patients in this group denied the existence of their affected extremities or were unable to identify parts of their involved extremities correctly. This phenomenon, called, among other things, autotopagnosia, was never the sole defect present and was not the defect upon which the evaluation of denial of illness was based. All these patients also had denial of illness. Even though they may have denied that the extremities were theirs, they stated that the ones they had were normal. The patients either could not identify the extremity when it was held up for their inspection or identified it as belonging to the examiner or someone else. One said, "I don't know what the hell it is!" They occasionally referred to it in inanimate terms, such as "dead wood." This defect sometimes took the form of an inability to identify fingers on the affected side. Taken by itself, such a finding suggests a finger agnosia or other aphasic or agnostic phenomenon, but the same patients give correct responses in regard to the unaffected side.

Absence of Aphasia: The patient may seem to have aphasia when the affected side is discussed. He may be unable to find the correct words, fail to carry out commands, become mute, or use neologisms or gibberish. When the normal side is tested, however, this apparent aphasia disappears. These phenomena did not occur in the patients who were aware of their illness. It is improbable that a disorder in language function, in the usual sense, can be implicated here. Furthermore, some patients with definite aphasia and right hemiplegia can clearly demonstrate, either verbally or by performance, that they are acutely aware of their physical defects. Weinstein has described "nonaphasic language disturbances" in patients with denial of illness.[4]

Denial of Associated Illnesses.—This phenomenon was not studied in the same detail as denial of the hemiplegia, but the patients generally did not deny other illnesses that could be verified, such as heart disease, arthritis, or hypertension. For example, several patients stated correctly that they had heart disease, while denying the more obvious and more recent hemiplegia. One patient had had a Parkinsonian tremor in the left upper extremity for 20 years as the result of carbon monoxide poisoning. With the onset of his hemiplegia the tremor disappeared, but he said he was in the hospital "to try to get rid of the tremor I have." Many of our patients were incontinent of urine, but only an occasional patient denied this symptom. As a matter of fact, although there were a few bizarre explanations for wetting the bed, some of the answers were astonishingly frank. One patient said, "I just let go, and I don't give a damn."

Denial of Illness by Others.—It is often stated, usually by the laity, but occasionally by physicians, that denial of illness occurs only because the patient has never been told that he is paralyzed and the sensory impairment in the involved limb prevents his becoming aware of this fact. In almost every case our patients

4. Weinstein, E. A., and Kahn, R. L.: Nonaphasic Misnaming (Paraphasia) in Organic Brain Disease, A. M. A. Arch. Neurol. & Psychiat. **67**:72-79, 1952.

were told directly and repeatedly that they were paralyzed, but this had no effect upon the responses. The daughter of one patient, overhearing her mother deny the existence of her hemiplegia in answer to our questions, interrupted the interview to explain why the patient answered as she did. "We told her she was all right, and she believes us. If I told her she was paralyzed, then she would answer your questions right." She talked to her mother, demonstrated to her that she was paralyzed, and invited us to repeat the questions. Again the patient stated she could move her left extremities and denied that they were paralyzed.

Denial of illness is also encountered in persons related to, or closely associated with, the patient. One of our patients was so aphasic that he could respond only to the simplest commands, but his physician insisted that he had normal speech function, saying, "He's really a nice guy. He's only excited and nervous now."

Patterns of Disorientation.—Weinstein and Kahn [5] found that disorientation in space and time usually follows a certain pattern in patients with brain disease. The directions of error were generally toward the patient's home, toward a happier time of day, or toward a time in which the patient was, or hoped to be, well. These patterns, in combination with the denial of illness itself, suggest a tendency toward a state of well-being exemplified by the home as contrasted with the hospital, the past as contrasted with the present, and absence of disease as contrasted with the current status. These findings were amply confirmed in this study, in which spatial disorientation, when it occurred, was always in the direction of the patient's home or toward a location less suggestive of illness than a hospital. That these patterns represent denial, and not lack of awareness, is evident from the spontaneous slips that occur in the conversation of these patients. One woman, aged 83, persistently claimed that she was home with her mother and father, but said spontaneously, "Doctor, will you come home with me and be my doctor when I get out of here?" Another woman maintained repeatedly, when questioned directly, that she was at home. In her conversation on other subjects, however, she indicated that she knew she was in a hospital. We asked her why she said she was at home when she knew she was in the hospital, and she replied, "Because I *want* to be home."

Another claimed that the hospital, which she named correctly, was in Buffalo, where she lived, and maintained that she was now "a couple of blocks from where I live." When told she was in New York City, she denied it. Later in the conversation, she was again asked where she lived, and she said, "Buffalo, when I'm home." This patient also showed "duplication," as observed by Weinstein in his series.[5] She maintained that there were several parts of Bellevue Hospital. One part she located correctly; the other part, "where I am now," she said was close to her home.

Some of these phenomena also occurred in the group without denial of illness. However, they were less common, did not take such bizarre forms, and were more susceptible of correction.

COMMENT

From the data presented, it is evident that denial of illness is fairly common. More than a quarter (28%) of the patients with hemiplegia showed this phenomenon. The actual incidence, however, is probably higher, since rigid criteria for

5. Weinstein, E. A., and Kahn, R. L.: Patterns of Disorientation in Organic Disease of the Brain, A. M. A. Arch. Neurol. & Psychiat. **65**:533-534, 1951; Patterns of Disorientation in Organic Brain Disease, J. Neuropath. & Clin. Neurol. **1**:214-225, 1951.

a single illness were used and many of the patients could not be tested because of severe aphasia. The percentages presented here merely represent the incidence of denial in a group of 100 consecutive patients observed under the conditions stated above. Observations on another group of hemiplegic patients, with the same methods of testing, might yield a lower or a higher incidence of denial of illness, depending on the number of cases of left and right hemiplegia, the number of cases of severe aphasia, the type of hospital (psychiatric or general), and, to a certain degree, the attitude of the investigators.

Expressions of denial of illness by the patient are often overlooked by the physician because they do not interest him or do not appear relevant to the symptoms of which the patient does complain. Many of our patients readily admitted that they were "sick" and described many unrelated symptoms, but stated flatly that nothing was wrong with their extremities, even when confronted with the fact that they were paralyzed.

From sporadic case reports that appear in the literature, one gains the impression that denial of illness is a rarity, although Gerstmann [1m] had already suggested that many patients may be found to show this abnormality if the examiner looks for it. By its very nature—denial—it will rarely appear spontaneously in the history but must be elicited by specific questions.

The difference in incidence of right and left hemiplegia was striking (3:1). Nielsen [6] classified this phenomenon among the symptoms of the "minor" hemisphere, although he stated that he had seen it in disease of the "dominant" side. In the present series, seven patients with right hemiplegia without aphasia expressed denial of illness. It is probable that this phenomenon is commoner in cases of severe aphasia than even these data indicate. Dattner,[7] by observing the imitation of gestures, showed that patients with severe aphasia are "confused" about the right side of the body and suggested that they lacked awareness of its defects.

Weinstein and Kahn indicated that the disorientation which occurs in these patients may merely be part of the whole pattern of denial of illness. Offhand remarks by many of our patients suggested that they actually knew where they were; yet when questioned formally as to orientation, they claimed that they were either in their homes or in other places more familiar to them than the hospital. It appeared, at least in some cases, that these patients were literally denying their location in time and space, rather than being actually unaware of it. Pointing out the patients' defects in the most concrete manner failed to alter the stated conviction that their extremities were normal. Weinstein and Kahn showed that all the phenomena observed—the denial of illness, disorientation, confabulation, and language difficulty—are part of an over-all pattern of behavior which appears at certain levels of defective brain function.

Often when other illnesses were present in addition to the hemiplegia, only the hemiplegia was denied. One patient, whose long-standing Parkinsonian tremor disappeared with the onset of the hemiplegia, denied the paralysis and maintained

6. Nielsen, J. N.: Agnosia, Apraxia, Aphasia: Their Value in Cerebral Localization, Ed. 2, New York, Paul B. Hoeber, Inc., 1946, pp. 82-84; 137-138.

7. Dattner, B.: Body Image Disturbances with Lesions of the Dominant Hemisphere, Tr. Am. Neurol. A. **75**:141-143, 1950.

that he still had the tremor. On the other hand, denial of illness, deafness, incontinence, and other symptoms can occur in association with denial of hemiplegia. We do not have sufficient information for worth-while speculation on this point.

In general, the productions of the patients with denial of illness closely resemble those in normal persons when explaining away or rationalizing any defect. The only differences are in degree and in susceptibility to correction.

SUMMARY

1. The incidence of denial of illness was found to be 28% on investigation of 100 consecutive cases of hemiplegia due to organic disease of the brain.

2. Denial of illness was always associated with an "organic mental syndrome" and occurred in a much higher proportion of cases of left hemiplegia. It also occurred, however, with lesions of the "dominant" hemisphere.

3. Associated phenomena, such as rationalizations, confabulations, duplications, denial of the existence of an extremity, denial of other illnesses, patterns of disorientation, and denial of the patient's illness by others, were observed and described.

STUDIES ON A PROTEOLYTIC ENZYME SYSTEM IN SCHIZOPHRENIA

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DURING our investigations on the protein metabolism of schizophrenic patients, a number have been found who exhibited a specific, pathological pattern of emotional response to stress and abnormally high concentrations of a proteolytic-enzyme inhibitor in the serum. The studies of West and associates [1] have demonstrated a relationship between the concentrations of this substance, rennin (human pepsin) inhibitor, and those of another, chymotrypsin inhibitor, and the rate of growth of cancer. The higher the titer of rennin inhibitor and the lower that of chymotrypsin inhibitor, the slower is the growth of the neoplasm. On the other hand, if the concentration of chymotrypsin inhibitor approaches or exceeds that of rennin inhibitor, the rate of growth is proportionately increased. Comparable relationships have been found between the relative concentrations of these enzyme inhibitors in active and in arrested pulmonary tuberculosis.[2]

Acute infections, physical traumas, and burns are accompanied by high chymotrypsin- and low rennin-inhibitor titers. Anxiety states, as reactions to immediate, acute stresses, also follow this pattern when unaccompanied by hysterical defenses.[3] On the contrary, high rennin- and low chymotryspin-inhibitor titers occur in a variety of chronic diseases. Pregnancy, hyperthyroidism, and, in some cases, hypertension are associated with significantly elevated rennin-inhibitor titers with a somewhat increased chymotrypsin-inhibitor titer.[4] West and associates, in establishing the normal values for these proteolytic-enzyme inhibitors, noted the consistent occurrence of high rennin- and normal chymotrypsin-inhibitor titers in childhood.[4]

The observation by one of the authors (C. E. T.) that the high concentrations of rennin inhibitor in the sera of schizophrenic patients occurred most frequently in the catatonic group suggested the importance of defining precisely the psychiatric

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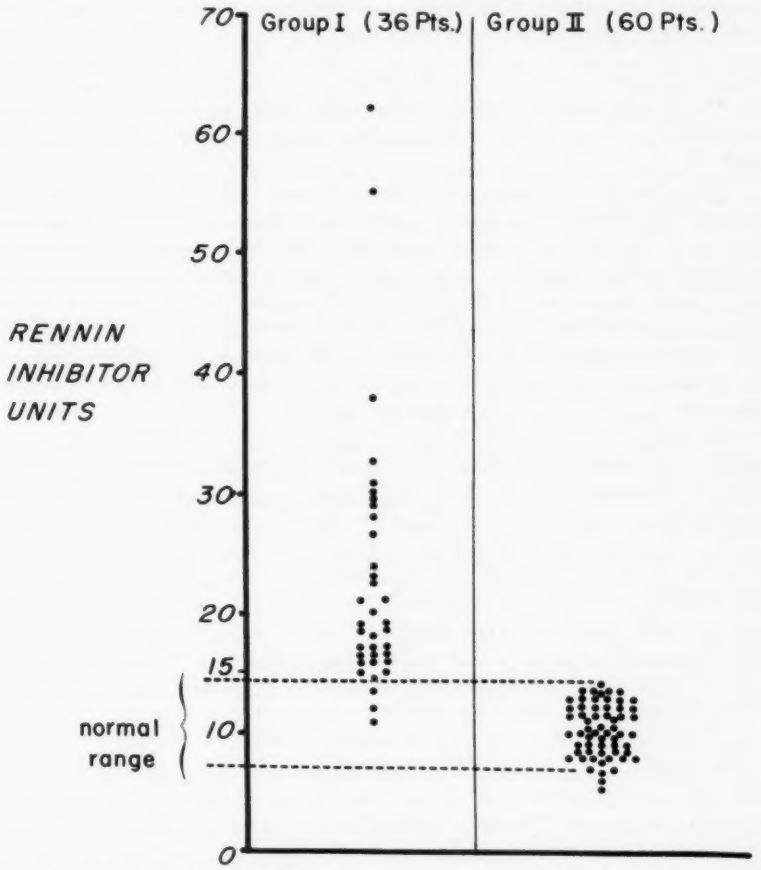
1. West, P. M., and Hilliard, J.: (*a*) Ann. West. Med. & Surg. **3**:227, 1949; (*b*) Proc. Soc. Exper. Biol. & Med. **71**:169, 1949. (*c*) West, P. M.; Rapaport, S. I., and Tempereau, C. E.: Cancer **4**:177, 1951.

2. Escovitz, W. E.: Personal communications to the authors.

3. Jacobs, J. S. L.; West, P. M., and Tempereau, C. E.: Proc. Soc. Exper. Biol. & Med. **78**:410, 1951.

4. West, P. M.; Hilliard, J., and Mietus, A. C.: Surg., Gynec. & Obst. **92**:209, 1951.

syndrome accompanying this biochemical abnormality. A direct association was found to exist between an increased rennin-inhibitor titer and the following emotional reaction pattern: (1) chronically low tolerance to frustration; and (2) the rapid or immediate appearance of confusion, obnubilation, amnesia, fugue, syncope, or stupor, as dissociative symptoms, in response to the type of external stress



Division of 96 male schizophrenic patients into two groups on the basis of the presence or absence of the formulated reaction pattern.

which would be conducive to the production of intensely hostile feelings, but which in this syndrome evokes transitory, slight, or no recognition of hostility.

METHOD AND MATERIAL

Ninety-six male schizophrenic patients were chosen consecutively from patients admitted to the psychiatric wards. Only patients were included who had received no physical psychiatric treatment in the past and who exhibited no evidence of physical illness. Corroborative diagnoses

were obtained by two or more psychiatrists. Confused patients, (four) were included only when unequivocal substantiating data were obtained from their families. Psychoneurotic patients and patients with latent and incipient schizophrenia were excluded from this study. Eight or more daily morning determinations of rennin and chymotrypsin inhibitors were obtained prior to any therapy or physical procedures on 92 of the schizophrenic patients. In the remaining subjects fewer determinations had revealed increased rennin-inhibitor titers. All biochemical studies were performed in the laboratory of Dr. P. M. West, at this hospital, according to methods described by him in 1949.[1b] Normal titers of rennin inhibitor in the male range from 7 to 14 units per 100 cc. The method is reproducible to within 1 unit.

RESULTS

The 96 schizophrenic patients were divided into two groups: (1) 36 who satisfied both criteria of the formulation described, and (2) 60 who did not satisfy both criteria.

The accompanying Figure demonstrates division of the patients into these two groups. When their maximum rennin-inhibitor titers are plotted, a significant correlation is found between an abnormally high concentration of this enzyme inhibitor and the fulfilment of both criteria of the formulation. However, the presence of dissociative symptoms or a low tolerance to frustration alone was unaccompanied by this biochemical abnormality. Two patients of the second group who had responded with intense anger and dissociative symptoms to delusions of reference and infidelity, but who had not demonstrated this reaction to external stimuli, exhibited normal rennin-inhibitor titers.

In general, the highest titers were obtained in patients with catatonic schizophrenia who displayed classic states of stupor or excitement. The distribution in both groups bore no relation to the remaining classifications of schizophrenia. No correlation was found between an abnormally high concentration of rennin inhibitor and the following signs and symptoms, singly or in combination: impulsiveness, loss of control over hostile impulses, assaultiveness, destructiveness, overwhelming hostile feelings, anxiety, delusions, and hallucinations. Similarly, the mood, the affective and intellectual status, changes in weight or libido, and the chronicity of the illness did not correlate with this enzymatic disturbance. No specific neurotic defenses appeared to be associated with it except so far as the formulation denoted.

COMMENT

It should be stressed that the schizophrenic patients who were studied were all men, between 22 and 44 years of age. Seventy-six had been psychotic for 5 to 10 years; 24 showed evidence of deterioration. Precipitating factors were often operative up to the time of admission. It is interesting in this respect that the highest rennin-inhibitor titers were usually found during the first few days of hospitalization. Thereafter, the rennin-inhibitor values sometimes decreased temporarily into the normal range, only to become elevated again in the presence of stress.

Within the hospital these patients were exposed to two general types of stress. In the first category were electric convulsion therapy, sedation and insulin coma therapy, and the intravenous administration of glucose, corticotropin, or epinephrine. The second category comprised psychiatric and psychodiagnostic examinations,

transfer from open to closed wards, and the anticipation of undergoing electric convulsion or insulin coma therapy or of taking a trial visit at home. This second group of stresses was sometimes accompanied by elevations in rennin-inhibitor titers, but only in patients who satisfied the complete formulation. Many patients, notwithstanding their group, exhibited this enzymatic change when subjected to any of the physical stresses mentioned, but this elevation was much more frequent and pronounced among patients within the formulated reaction pattern. Unquestionably, in some cases, the administration of physical procedures or therapies constituted threats which provoked hostility. Under controlled conditions, all patients subjected to psychological stresses conducive to the production of intensely hostile feelings who exhibited elevations of rennin-inhibitor levels belonged to the group of 36 who satisfied both criteria of the formulation.

Earlier attempts [5] to relate enzyme kinetics to mental status provided results which were suggestive of abnormalities, but not definitive. The metabolic significance of rennin inhibitor is unknown. It may be increased in a variety of chronic illnesses. High titers occur with a significant degree of consistency in patients with arrested cancer or inactive pulmonary tuberculosis. Under these circumstances the stress is prolonged and relatively constant. In childhood high titers of rennin inhibitor are the rule. The transition from the immature to the mature pattern occurs between the ages of 16 and 21.[4] It is generally agreed that the characteristic total biological response to chronic stress is the adoption of relatively undifferentiated, immature, regressive defenses. The satisfaction of both criteria of the formulated reaction pattern defines a most primitive form of ego defense. Psychopathologically, this pattern of behavior appears in infancy. The findings in these schizophrenic patients indicate a high correlation of immature, weak ego defenses and an immature pattern of enzyme kinetics. It will be pertinent to investigate psychiatrically the emotional status of those patients with chronic illness who exhibit elevated rennin-inhibitor titers. Studies are now being conducted with a group of psychoneurotic patients. These, and investigations of the effects of corticotropin, epinephrine, and glucose, will be reported in subsequent communications.

Over three-fourths of the schizophrenic patients studied belonged to the so-called ambulatory group. The remission rate following therapy was high. Most of them were able to resume social and occupational responsibilities. It is recognized that persons such as these comprise a significant proportion of the general population. Examination of the life histories of the patients who satisfied both criteria of the formulation revealed a high frequency of antisocial acts which were associated with confusion, amnesias, and fugues. Assaultiveness, destructiveness, sexual offences, and military transgressions, accompanied by such dissociative symptoms, were often recounted by patients in this group. It seems reasonable to assume that should the findings reported in this paper be confirmed for large numbers of persons, they may be of sociologic and forensic value.

SUMMARY

In a study of 96 physically healthy, schizophrenic male patients, abnormally high rennin-inhibitor titers were encountered only in those who exhibited the following

5. Langfeldt, G.: The Endocrine Glands and Autonomic Systems in Dementia Praecox: Clinical and Experimental Investigations, Bergen, J. W. Eide, 1926.

emotional reaction pattern: (1) chronically low tolerance to frustration; and (2) the rapid or immediate appearance of confusion, obnubilation, amnesia, fugue, syncope, or stupor, as dissociative symptoms, in response to the type of external stress which would be conducive to the production of intensely hostile feelings, but which in this syndrome evokes transitory, slight, or no recognition of hostility.

It is concluded that these findings indicate a high correlation of immature, dissociative ego defenses and an immature pattern of enzyme kinetics in schizophrenia.

James Eatinger, Virginia Hansen, Willard Keye, Bronnetta Scott, Reed Severin, and Ruth Ruderman gave technical assistance.

ANALYSIS OF CEREBRAL CONTROL OF REFLEX PUPILLARY DILATION IN CAT AND MONKEY

WILLIAM CROSBIE WILSON, M.D.
CHICAGO

THE PATHOGENESIS of inequality of the pupils following cerebral trauma is controversial. In 1878 Hutchinson described the unilaterally dilated fixed pupil in victims of head trauma.[1] He suggested impairment of the oculomotor nerve as the causative factor, and subsequent workers suggested the same etiological mechanism.[2] However, this explanation is not always applicable. In over two-thirds of a series of 450 cases of head trauma studied, the unilateral dilated pupil reacted well to a light stimulus, indicating that the oculomotor nerve was not completely functionless; furthermore, subsequent necropsy revealed no gross or microscopic damage to the oculomotor nerve.[3] Other observations suggested a cerebral mechanism.[3]

Several investigators have studied cerebral effects on the pupil from the physiological standpoint. Pupillary dilation in animals following cerebral electrical stimulation was reported first by Bochefontaine.[4] Soon thereafter substantiating observations appeared.[5] By 1900 Sherrington's work on dogs and revealed that pupillary dilation following cerebral excitation was due to inhibition of parasympathetic activity.[6] Succeeding work on cats and dogs has confirmed his observation.[7]

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From the Department of Physiology, the Stritch School of Medicine and the Graduate School of Loyola University.

1. Hutchinson, J.: Notes on the Symptom-Significance of Different States of the Pupil, Brain **1**:1, 1878; Sir Jonathan Hutchinson: Biography, M. Classics **5**:109-245, 1940.

2. Jefferson, G.: The Tentorial Pressure Cone, Arch. Neurol. & Psychiat. **40**:857-876, 1938. Meyer, A.: Herniation of the Brain, ibid. **4**:387-400, 1920. Rowbotham, G. F.: Acute Injuries of the Head: Their Diagnosis, Treatment, Complications and Sequels, Baltimore, Williams & Wilkins Company, 1945, p. 75.

3. Wilson, W. C.: The Unequal Pupil in Head Injury: A Clinicopathological Study, Arch. Neurol. & Psychiat. **61**:385-401, 1949.

4. Bochefontaine, M.: Contribution a l'étude des effects produits par l'excitation electique du cerveau, Compt. rend. Soc. biol. **27**:324-329, 1875.

5. von Bechterew, W. and Mislawski, N.: Über die Innervation und die Hirncentren der Thränenabsonderung, Neurol. Centralbl. **10**:481, 1891. Ferrier, D.: The Functions of the Brain, Ed. 2, London, Smith, Elder & Co., 1886. François-Franck: Leçons sur les fonctions motrices du cerveaus et sur l'epilepsie cérébrale, Paris, Gaston Doin & Cie, 1887. Luciani, L., and Tamburinini, A.: Studii clinici sui centri sensori corticali, Ann. univ. di. med. e chir. **247**:293-306, 1879. Shafer, K.: Experiments on Special Sense Localization in the Cortex, Cerebri of the Monkey, Brain **10**:362, 1888.

6. Sherrington, C. S.: Experimentation on Emotion, Nature **62**:328-331, 1900.

7. (*a*) Gellhorn, E., and Levin, J.: Nature of Pupillary Dilatation in Anoxia, Am. J. Physiol. **143**:282-289, 1945. (*b*) Hodes, K., and Magoun, H. W.: Pupillary and Other Responses

(Footnote continued on next page)

However, Karplus and Kriedl [8] reported the existence of a sympathetic subcortical pupillodilator center in the cat's tuber cinereum under orbital-gyrus control.

The purpose of the present study was threefold: (1) to determine whether the sympathetic and/or the parasympathetic system is active in cats and monkeys in the production of mydriasis following cerebral excitation, (2) to identify the pathway which the impulses follow from cortex to iris, and (3) to estimate the degree of activity of the pupillary light reflex during stimulation of cerebral pupillodilator areas.

METHODS AND TECHNIQUES

Fourteen cats and 4 rhesus monkeys were used in the exploration of the cerebrum for pupillodilator areas and pathways. Sacrifice experiments were performed; diallylbarbituric acid (dial®[9]) anesthesia, induced by intraperitoneal injection of the drug, 80 mg. per kilogram of body weight, was used. The cerebrum was exposed and the head fixed to a stereotaxic apparatus, which was used to place a bipolar concentric needle electrodes at millimeter intervals throughout the rostral three-quarters of the right cerebrum. The stimulus consisted of one-second volleys of a 60-cycle alternating current of 3 to 6 volts. The pupillary responses were observed through a lens with a magnification of two, and were recorded by the observer as mild (2 to 3 mm.), moderate (3 to 5 mm.), and marked (5 to 8 mm.). After each exploration coronal sections of the cerebrum were made at 10 μ thickness, and every tenth section was stained by the Weil technique. The sections were projected on millimeter paper; the particular anatomical structures stimulated were identified and correlated with their pupillary responses.

In order to study the reflex pathways, an acute right cervical chain sympathectomy was made on four cats and two monkeys; an acute right ciliary parasympathetic ganglionectomy was made also on four cats and two monkeys; a combination of the two operations was performed on two cats.

Light reflex activity was tested by directing a beam of light (intensity of 100 f-c.) into the left pupil at a distance of 6 in. (15 cm.) with alternate cerebral stimuli.

RESULTS

Stimulation of Pupilloexcitatory Areas in Cats.—The results of a representative experiment, seen in Figure 1, indicate the location of the frontal-lobe pupilloexcitatory areas. The gyrus proeus, gyrus genualis, and gyrus subcallosus were involved in all cat experiments.[10] When these areas were excited on the right side only, mild to moderate mydriasis occurred. The duration of a typical response is seen in Figure 2 (dotted-line curve). On the other hand, the result of stimulation of sympathetic areas in the hypothalamus was pronounced mydriasis, accompanied by retraction of the nictitating membrane, piloerection, and baring of the fore claws; in the mydriasis due to hypothalamic excitation the latent period was not discernible (Fig. 2, broken-line curve).

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from Stimulation of Frontal Cortex and Basal Telencephalon of the Cat, J. Comp. Neurol. **76**:461-473, 1942. (*c*) Parsons, H.: On Dilatation of the Pupil from Stimulation of the Cortex Cerebri, J. Physiol. **26**:366, 1901. (*d*) Ury, B., and Oldberg, E.: Effect of Cortical Lesions on Affective Pupillary Reactions, J. Neurophysiol. **3**:201-213, 1940. (*e*) Wang, G. H.; Lu, T. W., and Lau, T. T.: Pupillary Dilatation from Cortical Stimulation, Chinese J. Physiol. **6**:225-233, 1932.

8. Karplus, J. P., and Kriedl, A.: Gehirn und Sympathicus: Zwischenhirn Basis und Hals sympathicus, Arch. ges. Physiol. **135**:129-138, 1909; Ein Sympathicuszentrum im Zwischenhirn, ibid. **135**:401-416, 1910.

9. We are indebted to the Ciba Pharmaceutical Products, Inc., Summit, N. J., for the generous supply of dial® used in this work.

10. Throughout the text these gyri will be called collectively the frontal lobe.

Selective Iris Denervation in Cats.—Selective autonomic-nerve sections were made to show whether cerebral excitation activated the pupil through the sympathetic or the parasympathetic system.

Right ciliary parasympathetic ganglionectomy was made on four cats, resulting in dilation of the right pupil to 7 mm.. This pupil reacted as before the denervation. However, upon hypothalamic stimulation both pupils responded, as shown in Figure

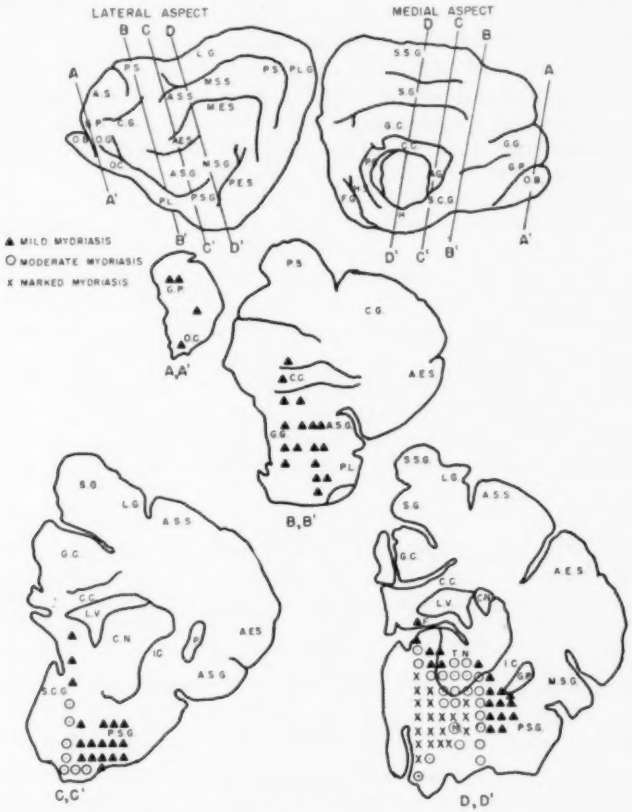

Fig. 1.—Effects on mydriasis of stimulation of pupilloexcitatory areas of the frontal lobe in the cat.

A.C. indicates anterior commissure; *A.E.S.*, anterior ectosylvian gyrus; *A.S.*, anterior sigmoid gyrus; *A.S.G.*, anterior sylvian gyrus; *A.S.S.*, anterior suprasylvian gyrus; *C.C.*, corpus callosum; *C.G.*, coronal gyrus; *C.N.*, caudate nucleus; *D.G.*, dentate gyrus; *F.*, fornix; *F.G.*, fusiform gyrus; *G.C.*, gyrus cinguli; *G.G.*, gyrus genualis; *G.P.*, gyrus proeus; *H.*, hypothalamus; *H.G.*, hippocampal gyrus; *I.C.*, internal capsule; *L.G.*, lateral gyrus; *L.O.T.*, lateral olfactory tract; *L.V.*, lateral ventricle; *M.E.S.*, middle ectosylvian gyrus; *M.S.G.*, middle sylvian gyrus; *M.S.S.*, middle suprasylvian gyrus; *O.B.*, olfactory bulb; *O.C.*, olfactory crus; *O.G.*, orbital gyrus; *P.*, putamen; *P.E.S.*, posterior ectosylvian gyrus; *P.L.*, pyriform lobe; *P.L.G.*, posterior lateral gyrus; *P.S.*, posterior sigmoid gyrus; *P.S.G.*, posterior sylvian gyrus; *P.S.S.*, posterior suprasylvian gyrus; *S.C.G.*, subcollasol gyrus; *S.G.*, splenial gyrus; *S.S.G.*, suprasplenial gyrus, and *T.N.*, thalamic nucleus.

2 (broken line). Both pupils reacted maximally to an intravenous injection of 0.5 cc. of 1:1,000 epinephrine hydrochloride. The pupils returned to the post-denervation resting state in three minutes.

Right cervical chain sympathectomy was performed on four cats. Excitation of the right frontal lobe caused normal mydriasis, as seen in Figure 2 (dotted line). Hypothalamic stimulation caused the normally innervated left pupil to dilate maximally, as seen in Figure 2 (broken line) and the right pupil to dilate moderately, as seen in Figure 2 (dotted line). Intravenous injection of 0.5 cc. of 1:1,000 epinephrine hydrochloride caused a similar reaction to the first injection mentioned above.

Right ciliary ganglionectomy and right cervical sympathectomy were performed on two cats. The denervated (right) pupil assumed a diameter of 4 mm. and remained fixed throughout the cerebral exploration. The intact (left) pupil behaved

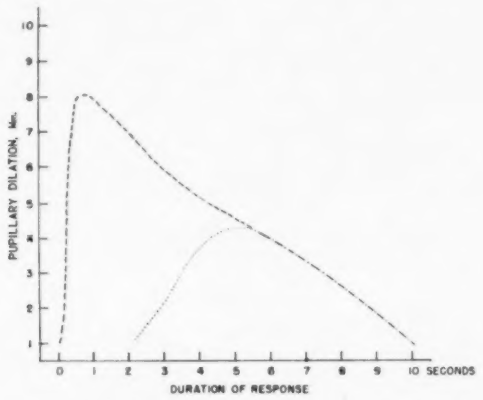

Fig. 2.—The broken line indicates a representative pupillary (sympathetic) response following hypothalamic stimulation; the dotted line represents the pupillary (parasympathetic) reaction of the sympathectomized cat, normally hidden in the intact preparation.

in the normal manner. Again, injection of epinephrine hydrochloride caused pronounced mydriasis and slow recovery to the size of the resting pupil.

Stimulation of Pupilloexcitatory Areas in Monkeys.—Excitation of the arcuate gyrus caused mydriasis with or without conjugate eye movements (the eye-movement response was dependent upon current strength and location of cortical points stimulated). The resting pupil, measuring 2 to 3 mm., rapidly dilated to about 8 mm. after a variable latent period, with a rapid return to the resting size.

Selective Iris Denervation in Monkeys.—Right cervical chain sympathectomy abolished the ipsilateral pupillary response to stimulation of the arcuate gyrus. Right ciliary ganglionectomy had no effect on the normal pupillary reaction initiated by cerebral excitation. This reaction was unaffected by varying the depth of diallyl-barbituric acid narcosis. Two monkeys were used in this study.

Light Reflex.—The cat's light reflex was abolished during excitation of the frontal lobe, with immediate restoration of light-reflex activity following cessation

of stimulation. The presence of light directed into the eye caused about a 25% reduction in mydriasis resulting from excitation of the hypothalamus in the cat and the arcuate gyrus in the monkey.

COMMENT

The results in cats substantiate the existence of cerebral pupillodilator areas functioning by inhibition of the parasympathetic activity, confirming the observations of Hodes and Magoun.[7b] It is demonstrated that the excitatory areas are found in the gyrus proeus, gyrus genualis, and gyrus subcallosus. The subsequent passage of these impulses through the hypothalamus is suggested by the physiological dissection (Fig. 1). Further indication that these frontal lobe fibers traverse the hypothalamus is seen as a result of the selective denervation experiments. After hypothalamic stimulation the intact (left) pupil responded by maximal dilation, accompanied by overt sympathetic discharge, as seen in Figure 2 (broken line). The later reaction probably resulted from excitation of the frontal lobe projections as they traverse the hypothalamus in their course to the Edinger-Westphal nucleus. In normally innervated pupils the "dotted-line" response is masked by the dominant sympathetic activity.

The method of exploration utilized failed to disclose the area on the medial surface of the cat's frontal lobe, reported by Siebens and Woolsey, which evokes reciprocal activity of the sympathetic and parasympathetic innervation of the pupil.[11] The dominant mechanism for producing mydriasis from the cat's frontal lobe appears to be active parasympathetic inhibition, whereas the sympathetic component is dominant in monkeys, confirming the observations of Ward and Reed.[12]

The abolition of the light reflex in cats during stimulation of the frontal lobe suggests that the Edinger-Westphal center is actively inhibited during cortical excitation.

SUMMARY

Cerebral pupillary dilation follows adequate excitation of the gyrus proeus, gyrus genualis, and gyrus subcallosus in cats and the arcuate gyrus in monkeys.

Frontal-lobe mydriasis is due to active inhibition of parasympathetic activity in monkeys.

Evidence indicates that centrifugal frontal lobe fibers controlling mydriasis by active inhibition of parasympathetic activity pass through the hypothalamus to terminate in the Edinger-Westphal nucleus.

The light reflex is inhibited during frontal-lobe elicitation of mydriasis in cats.

11. Siebens, A., and Woolsey, C. N.: Cortical Autonomic Center for the Eyes on the Mesial Surface of the Frontal Lobe in Cat, Federation Proc. **5**:95, 1946.

12. Ward, A. A., and Reed, H. L.: Mechanism of Pupillary Dilatation Elicited by Cortical Stimulation, J. Neurophysiol. **9**:329, 1946.

Society Transactions

CHICAGO NEUROLOGICAL SOCIETY

Hugh T. Carmichael, M.D., *President, in the Chair*

Regular Meeting, March 11, 1952

Fusion Versus Nonfusion in Operative Treatment of Protrusion of an Intervertebral Disk. Dr. Harold C. Voris and Dr. Joseph T. Coyle.

The authors reported a series of 244 cases of protrusion or suspected protrusion of a lumbar intervertebral disk in which 274 operations were performed. The protrusions were at the fifth lumbar-first sacral level in 88 cases (39%), at the fourth-fifth lumbar level in 114 cases (52%), at the third-fourth lumbar level in 17 cases (8%), at the second-third lumbar level in 2 cases, and at the first-second lumbar level in 1 case. The protrusions were at more than one level in 16 cases. In one case there were three protrusions.

Reflex disturbances were present in 55% of the cases in which a disk protrusion was found and in 42% of the cases in which exploration showed no protrusion. Sensory disturbances were present in only 27% of the cases of disk protrusion and in 30% of the cases in which no protrusion was found. Contrast myelography was carried out with ethyl iodophenylundecylate (pantopaque®) or iodized oil U. S. P. (lipiodol®) in 169 cases. It revealed defects indicating disk protrusions which were later identified at operation in 121 cases (72%), but led to an incorrect diagnosis in 48 cases (28%).

The result was considered good when the patient returned to his former activity without any complaints, or only occasional mild low-back or sciatic pain. The result was called fair when the patient returned to his former activity but complained of low-back or sciatic pain on occasion. Such patients were never incapacitated. If the patient was not able to resume his former activity or was incapacitated, even if only occasionally, the result was considered poor. There were four deaths. Two of these were due to meningitis. One patient died of pulmonary embolism as she was leaving the hospital, after an apparently satisfactory convalescence. The fourth patient died of peritonitis following rupture of the appendix.

Good to fair results were obtained in 87% of all patients. There was no significant difference between the group in which spinal fusion was done and that in which it was not. Of 34 patients who were operated on while the question of compensation or liability was still undetermined, good results were obtained in only 50% and fair results in 29%. Of 13 patients of the group who had fusions, good or fair results were obtained in 84%, while of 21 patients who did not have fusion there was a good to fair result in only 64%. Of 50 cases in which exploration did not reveal protrusion, good to fair results were obtained in only 66%. However, in 29 of these operations fusion was performed, with good to fair results in 69%. Of 21 cases in which exploration revealed no protrusion and fusion was not done, good to fair results were obtained in 61%.

DISCUSSION

Dr. Paul Bucy: It has not been my custom to do fusion of the spine in as high a percentage of cases as have Dr. Voris and Dr. Coyle. I must say that I do not believe a study like this gives us the answer as to which is the better procedure. In this series the surgeons have selected cases in which they think fusion should be done; obviously, these cases must have presented some differences from those in which they did not do fusion. Therefore the two groups of cases are not the same and are not comparable. If, on the other hand, we do compare them, it is equally obvious that the results are so nearly similar as to raise a question as to the value of the fusion. It is true there was a slight difference, but I doubt whether the differences are statistically valid.

Dr. Adrien H. Verbrugghen: My colleagues and I have operated in about 600 cases of protruded intervertebral disk in the lumbar region, and we have done spinal fusion in about 200 more. In the first 200 cases in which operation was performed for the syndrome of herniated

lumbar disk, fusion was not considered. These 200 cases have been followed rather carefully, and there is information on 167. In six cases spinal fusion was done either by us or by others because of persistent low-back pain, and in 10 others the patient would probably benefit from fusion, for the same reason.

After completion of this series, an attempt was made to select patients with the lumbar-disk syndrome for whom fusion might be indicated. The main factors were chronic backache between bouts of sciatica and a long history (over three years) of backache preceding the onset of acute symptoms of protruded disk. Patients with congenital anomalies of the lower back with sciatica also had fusion. Although the study of the 200 patients who had fusion is not complete, it may be noted that the results in 10 of these, for various reasons, were not satisfactory. This suggests that an unsatisfactory result, as far as relief of backache is concerned, may be expected in our group.

On three occasions, and with three different orthopedic surgeons, I have removed disks from under a vertebral fusion. This is a tedious, and sometimes difficult, procedure.

Fusion is, therefore, not a panacea for the syndrome of the protruded lumbar intervertebral disk. I must agree, however, with the opinion expressed by Dr. Voris that the best results will probably be obtained when the orthopedic surgeons and neurosurgeons cooperate, both in consultation and in operative treatment.

Dr. Harold C. Voris: Dr. Bucy, of course, is right in his comments, in view of the provocative nature of our title. It is apparent to everyone that we did not prove which was better, fusion or nonfusion. We have satisfied ourselves that there is a group of patients for whom fusion is not necessary. Unfortunately, from this point on, the decision becomes a matter of individual experience and judgment. We do not believe, however, that all the cases fall into one or the other of these groups. That would mean either that a great many unnecessary fusions are performed or that many patients who need fusion would get it only at the cost of another operation, with its additional expense, risk, and loss of time.

Diencephalic Dysrhythmias in Patients with Peptic Ulcer and Functional Gastric Disorders. Dr. Walter R. Kirschbaum and Dr. Howard C. Stehle.

The prominent role of the highest integrating psychosomatic centers in the causation and the recurrence of peptic ulcer and functional gastric disorders has been universally recognized. Final proof of the neurogenic theories of peptic ulcer is lacking. It appeared worth while to approach the problem electroencephalographically.

The study was based on the histories and the repeated medical, roentgenologic, neuropsychiatric, and electroencephalographic examinations of 60 consecutive patients of the Veterans Administration, Regional Office clinics, Chicago, whose course was followed for 5 to 10 years.

Of 50 patients with peptic ulcer, 45 (90%) had normal electroencephalographic patterns; 2 (4%) had nonparoxysmal fast activity; 3 (6%) had paroxysmal 6- and 14-per-second spike discharges suggesting thalamic or hypothalamic involvement (Gibbs and Gibbs). It is interesting that in the last group some patients presented clinical manifestations which independently suggested disturbances in the regulatory mechanisms of the diencephalon.

Of 10 additional patients without x-ray evidence of peptic ulcer, but with strong psychoneurotic features, 8 had normal electroencephalograms; none had nonparoxsymal electroencephalograms, and 2 had paroxysmal 6- and 14-per-second spike discharges. The clinical manifestations of the patients with the spike discharges also suggest imbalance of diencephalic centers.

As reported by Gibbs and Gibbs, the 6- and 14-per-second spike patterns were recorded in only 2% of control subjects but were found in 6% of patients with a clinical history of epileptiform disorder.

The relatively frequent occurrence of the 6- and 14-per-second spike discharges in patients with gastrointestinal symptoms suggests a possible correlation of gastric disturbances and thalamic or hypothalamic dysrhythmia.

DISCUSSION

Dr. F. A. Gibbs: For a time, I thought the authors were going to discover a high degree of correlation of peptic ulcer and 14- and 6-per-second spike discharges (suggesting diencephalic disorder). However, their final statistics do not show a high correlation. I believe, nevertheless,

that they have found an important relation, which, though not simple, is entirely reasonable. From what is known clinically, one should be prepared for their conclusion that peptic ulcer is not simply a form of diencephalic epilepsy. However, it is reasonable to suppose that in persons with a predisposition to ulcer structural changes clearly definable as peptic ulcer would be likely to develop if they also had disorders of gastric motility and secretion with nausea and vomiting on a basis of epilepsy. It would be astonishing if in a large group of patients with x-ray evidence of peptic ulcer a few did not show electroencephalographic evidence of diencephalic epilepsy, and in this group diencephalic epilepsy could reasonably be considered a contributing cause, or at least a probable exacerbating factor.

A small number of epileptic patients have gastric pain and vomiting associated with clinical and electroencephalographic evidence of diencephalic epilepsy. These patients come to an epilepsy clinic instead of a gastroenterological clinic because, in addition to purely visceral disturbances, they have black-out spells or convulsions, but diencephalic epilepsy is not necessarily associated with attacks of unconsciousness. Patients with diencephalic epilepsy and without attacks of unconsciousness are likely to find their way to a gastroenterological clinic, with the presumptive diagnosis of peptic ulcer. In the consultation clinic for epilepsy we have seen three cases in which the diagnosis of peptic ulcer was made by qualified clinicians, but in which 14- and 6-per-second positive spike discharges were found and all symptoms ceased when the patient was placed on anticonvulsant medication.

Misdiagnosis and inappropriate therapeutic efforts will result if a distinction is not made between peptic ulcer and diencephalic epilepsy, and similar confusion will arise if we fail to recognize that the two disorders can and do occur in some persons concurrently. When 14- and 6-per-second positive spikes are present, a therapeutic test with anticonvulsant medication may make it possible to distinguish between the epileptic and the nonepileptic components of the symptoms. In general, the type of epilepsy that is characterized by 14- and 6-per-second positive spikes is more sensitive to anticonvulsant medication than any other.

Dr. James L. O'Leary, St. Louis: One has to have a very wide base line in trying to evaluate cerebral activity. In every case in which there appears to be disturbance of brain activity, one should consider the normal for that particular family or history.

Dr. Walter R. Kirschbaum: We are aware that the problem is complicated and that too early conclusions should be avoided. As it appears, the problem of the pathogenesis of peptic ulcer has not been approached in electroencephalographic studies. An unusual opportunity appeared for the investigation of such organic and functional gastrointestinal disorders, and a surprisingly high percentage of diencephalic dysrhythmias was found. It is a matter of terminology whether or not the abnormal apparently thalamic and/or hypothalamic discharges should be called epileptic. We should like to suggest that special focal dysrhythmias may fire through the brain stem into the peripheral autonomic nervous system, reaching the gastrointestinal tract. Much depends on continuation of such studies by repeated electroencephalograms during the various phases of these gastric disorders, on a further analysis of the characteristic 6- and 14-per-second spikes as originating in the diencephalon, and on a sufficiently large material of normal controls.

Survey of Newer Experimental Observations upon Touch and Pain Pathways and Their Applications to Clinical Investigation. Dr. James L. O'Leary, St. Louis.

There are four types of sensory axons in peripheral nerve, all possible activators of forebrain, midbrain, and hindbrain centers. On the basis of the nerve-modality construction, the most rapidly conducting of these are proprioceptors, and tactile afferent fibers follow. Between tactile afferent fibers and the next slower group, of pricking-pain axons, there is a fourfold to sevenfold difference in threshold for direct electrical activation of nerve, thus making it possible to compare potentials evoked in the centers by stimulation of "tactile" and "tactile plus pricking-pain" groups. Between the small myelinated pricking-pain" afferent fibers and the nonmyelinated group, which mediates a slower, diffuse pain, there is a still greater disparity of threshold.

The modality concept, based upon anatomicophysiological correlations, is well established only to the first cell station. Just enough studies have been made on conduction in lemniscus systems to indicate the need for examining there further applications of this concept. For

clinical purposes, chief reliance must still be placed upon Marchi checks of the results of differential chordotomy in man. My recent experimental studies indicate that lemniscus axons representing thoracic and more caudal dermatomes enter the ventral white column mixed with propriospinal and with other afferent axons, which distribute to the reticular substance of the medulla. Many of the diffusing axons are of homolateral origin, whereas the lemniscus component is chiefly of contralateral origin. During ascent of the cord the loss of numerous propriospinal axons brings about a progressive concentration of the afferent components to higher centers; a lateral shift (Walker) also occurs. Usual schematics illustrating the topical distribution of pain-touch axons in the ventrolateral sector of the high cervical portion of the cord are erroneous in assigning equal proportions of the white matter to cervical and to sacral dermatomes; they are correct in indicating the concentration of afferent axons for pain in the ventrolateral sector. As lemniscus paths enter the lower part of the brain stem, they pass chiefly through the lateral reticular area and do not contribute significantly to the exterior fiber group. The latter is made up of the spinocerebellar paths. Many lemniscal axons are lost to the reticular substance of the medulla, indicating the possibility that the path for pain makes connections there with the diffuse reticular system described by Magoun and associates.

Subsequent to electrical stimulation of selected peripheral nerves in the cat, or to stimulation of hairs by agitation, a sharply focalized potential can be recorded from the contralateral ventral thalamic nucleus. The loci for sciatic and superficial radial nerves in the ventral thalamus are farther rostral than one might expect as a result of Marchi degeneration studies. The evoked potential thus recorded has a di- or triphasic form (Marshall), the initial positive phase being due to arrival of incoming lemniscus axons, and the next (negative) phase to the activity of thalamic cells discharging to the cortex. However, simultaneous recordings from somatic Area I of the cortex and the thalamic locus shows that the positive phase of the former commences just after that of the latter, suggesting that the postsynaptic discharge of the thalamus commences as soon as the first disturbance set up by the arriving lemniscus volley is transferred to postsynaptic elements. With due regard to the threshold and maximum values for the various axon components of peripheral nerve, it would appear that the entire rising phase of the evoked thalamic potential is accounted for by "tactile and proprioceptive" axon components alone. The "pricking-pain" delta axons of nerve appear to lengthen the initial positive phase. As yet we have not recorded a component of the evoked thalamic potential corresponding to activation of nonmyelinated peripheral axons.

DISCUSSION (IN PART)

DR. THEODORE B. RASMUSSEN: In these degeneration experiments in the monkey has Dr. O'Leary noted the appearance of spinothalamic fibers located dorsal to the dentate attachment? I have in mind a patient on whom my colleagues and I did a right-sided chordotomy at the third cervical segment and, 10 days later, a left-sided chordotomy at the second thoracic level for pelvic pain. Complete analgesia of the contralateral side followed the first procedure, but after the second procedure there was only moderate hypalgesia of the contralateral side.

The patient died from the malignant neoplasm shortly after, and serial sections through the chordotomy sites revealed at each complete degeneration of the anterolateral quadrant of the spinal cord on each side. We had to postulate, therefore, that the pain fibers still functioning lay dorsal to the dentate attachment.

DR. W. S. MCCULLOCH: I believe I understood Dr. O'Leary to say that the time for axonal conduction from the onset of the potential changes in the thalamus was the same as the time from their onset in the cortex when they were evoked by afferent stimulation. An old experiment by Dusser de Barenne, in which I assisted him, consisted of scooping out the thalamus at a time when strychnine spikes were appearing in the cerebral cortex after strychninization of the nuclei of the columns of Goll and Burdach and finding that these spikes continued to come through to the cerebral cortex. So far as I know, there is no proof that all the axons originate in these nuclei and in the thalamus. It may well be that some of them come through to the cerebral cortex. This may account for the absence of a thalamic delay. Have you ever considered repeating these experiments?

DR. GERHARDT VON BONIN: In the diagram of the spinal cord, the gelatinous substance was shown and then the tract went directly up the cord. Do you have any evidence as to the number of synapses in the posterior horn—in other words, on the timing of impulses traveling along the spinothalamic tract?

DR. JAMES L. O'LEARY, St. Louis: Dr. Rasmussen inquires whether the incision into the ventrolateral column of the cervical portion of the cord needs extend dorsal to the insertion of the denticulate ligament in order to achieve a satisfactorily high level of analgesia. In some cases, I believe, it is likely that it does, for in several procedures of Dr. Schwarz which I witnessed it was necessary to carry the incision somewhat more dorsally in its medial extent.

One discusser has inquired about the implications of the work presented with respect to Magoun's studies upon reticular activation of the cortex. It is my experience that the anatomically designated spinotectothalamic and spinoreticular systems are corepresented in the lateral reticular substance of the medulla. This association extends rostrally almost to the seventh cranial nerve nucleus, at which level most of the spinoreticular axons have terminated. Thus, it is possible that the lateral reticular region forms a link between the ascending sensory systems and Magoun's reticular activation mechanism. In fact, Petrén, whose early reliable clinical studies were mentioned by one of the discussers, believed it possible that there is a synapse in the pain pathway in the lateral reticular substance.

Other interesting points were brought up in the discussion. It will probably be a long time before the evoked potentiation equivalents for such concepts of clinical testing as vibration, number writing, and weight and form discrimination can be worked out so as to disclose the relative importance of analytical participation of the cortex and the thalamus. That possible outcome of the study of sensory paths by electronic methods is most readily visualized in number writing. The route for tactile sensibility from periphery to cortex is an outstanding example of the operation of "local sign" in the nervous system. Therefore, if one is willing to assume much greater precision in experimental control, to the point where activation of a few nerve fibers from one sensory spot are detected in the thalamus and cortex, it is possible that a corresponding design between a skin and a thalamic or cortical mosaic of points might be detected.

As to the causalgia-like syndrome which develops in cats after "alumina" (aluminum oxide) gel is injected about the high lumbar part of the cord, such animals may become much more irritable, and their reactiveness greatly exaggerated when they are disturbed on cleaning the cage or other manipulation. If they are then left alone for 10 to 24 hours and reexamined, it will be noted that their irritability is considerably reduced. Another period of handling is sufficient again to exacerbate the irritability over their hind extremities. It was also asked whether there is electrophysiological evidence for a homolateral spinothalamic tract. There is. Electrical stimulation of one of the sensory nerves gives a small, well-defined potential maximum in the ventral nucleus of the homolateral thalamus. However, by comparison, the evoked potential recorded from the contralateral thalamus is enormous.

With respect to Dr. McCulloch's question, I can only state that we are as yet unable to account for all the fibers of peripheral nerve in terms of various components of the potential complex activated in the contralateral thalamus and cortex. I believe that these will be proved to exist as more refined recording techniques become available.

Hugh T. Carmichael, M.D., *President, in the Chair*

Regular Meeting, May 24, 1952

Heredity Ataxia: Presentation of Three Cases (Siblings), with One Autopsy Report.

DR. HERMAN JOSEPHY.

Three of 11 siblings, offspring of unrelated parents, showed the first signs of cerebellar ataxia at about the age of 10 years. At the same time they deteriorated mentally. Finally, they exhibited the picture of severe ataxia with all cerebellar signs, combined with increased deep reflexes and a Babinski sign. The pupils reacted to light and in accommodation; the ocular fundus was normal, and vision was not impaired. Dementia was pronounced.

Two of the siblings are alive, at the ages of 30 and 40, respectively. The oldest one died at the age of 49. His brain exhibited advanced atrophy of the cerebellum. The pons, too, was small. The cerebral hemispheres had a normal appearance.

Microscopic examination revealed degeneration of the posterior tract in the cord. The cerebellar cortex exhibited severe degeneration of the granular layer. The Purkinje cells were well preserved.

Many, but not all, nerve cells in the spinal ganglia, the anterior horns, and the medulla oblongata were ballooned and filled with lipid granules. Some of the Purkinje cells were affected in the same way. In the hypothalamic nuclei ballooned cells were noted frequently. In the basal ganglia and the cerebral cortex most of the nerve cells had a normal appearance. However, here and there a cell was filled with lipid granules.

The clinical diagnosis was cerebellar ataxia combined with severe progressive dementia. Anatomically, the cases belonged to the group of late amaurotic familial idiocy "without amaurosis" and illustrate the wide range of varieties occurring in the lipidoses of the central nervous system.

Report on Psychosurgery Program at Chicago State Hospital. DR. ISADORE SPINKA, and DR. MILTON TINSLEY.

The psychosurgery program at the Chicago State Hospital was begun February, 1950. The report was on 56 patients, 35 of whom had prefrontal lobotomy, 6 a topectomy, and 9, a combined operation. Of these 56 patients, 16 showed marked improvement and are now at home, and 30, definite improvement and are making a better institutional adjustment. Ten patients were considered to show no improvement, but 5 of these have been operated upon within the past six months. Twenty-two had postoperative electroshock treatment, and 17 gave a favorable response. There was one death in this series, which occurred two weeks after operation. The cause of death was acute renal failure. Our best results were obtained with the standard open method of prefrontal lobotomy (Lyerly).

Patients selected for surgery were chronic disturbed schizophrenic patients, most of whom had had maintenance electroshock therapy with temporary improvement from the electroshock therapy. A special rehabilitation program, including group psychotherapy, is in effect for lobotomy patients.

In general, we are favorably impressed with our results and plan to expand our program.

DISCUSSION

DR. PERCIVAL BAILEY: In my opinion, lobotomy does change the fundamental personality of the patient; and for this reason we have done few such operations at the University of Illinois. Sooner or later someone will advise us as to whether lobotomy will change the personality of a patient. The patient cannot perform afterward as he did before. There are other defects. He cannot plan; he cannot carry out fundamental intellectual processes. I can see circumstances in which it would be advisable. In medicine, we are always trading one defect for another. We take out a piece of stomach. That is the way in which we have to look at this operation. After operation the patient's troubles will be less annoying than before.

DR. WARD C. HALSTEAD: I can support everything that has been said. I presume there are technical reasons that the results are what they are. However, we usually keep in mind that these patients do not represent favorable cases.

DR. ISADORE SPINKA: It must be remembered that we are dealing with patients who were psychotic and that they show a very decided improvement over their previous psychotic state. Some of them have gone home. I can read some reports of how these patients behave at home.

DR. PERCIVAL BAILEY: I am in entire agreement with you. I did not mean these patients have to teach geometry in a university; certainly, they are improved. Their personalities have changed, and for the better.

Psychiatric Problems in Displaced Persons. DR. GEORGE FENYES.

Fifty-one cases of psychosis in displaced persons admitted to a state hospital during the last three years were observed and evaluated. The patients came largely from East European countries. These displaced persons showed some similarities to the previous immigrant group of refugees. In contradistinction to them, however, they were pushed by circumstances to come here rather than deciding themselves to immigrate and they were inclined to consider their immigration as temporary only.

Social factors in this group of psychotic displaced persons were pointed out, especially their origin from agricultural countries, which made them more similar to the prewar immigrants.

Their previous traumatic experiences, poor social situation, and lack of knowledge of the language contributed to the paranoid psychosis which they developed.

The large number of depressive psychoses, especially refusal of food, pointed to the significance of oral factors and unresolved relations to the mother. The unconscious connections of mother, mother country, and mother language were pointed out, showing again the great significance of oral factors in their regressive psychosis.

There was a close correlation between the psychological and the social factors, which sometimes appeared as two sides of the same phenomena.

Social, psychological, and biological elements are highly integrated in the normal personality, mental illness meaning mainly the disintegration of these component groups.

Psychodynamic Differences Between Undetermined and Paranoid Types of Schizophrenia Elicited by the Projective-Movement-Sequence Test. MR. WILLIAM LUNDIN.

The projective-movement-sequence test is a projective device using a motion picture of eight scenes (20 to 55.5 seconds in length). In these scenes iron filings form various bizarre patterns, to which the subject's free associations are obtained. Twenty-five patients with an undetermined type and 25 patients with a paranoid type of schizophrenia of clear diagnosis were tested. These 50 patients were compared with 25 "well-adjusted" controls. Quantitative scores had been developed; qualitative interpretations were also made.

The following outstanding differences were found: Of the three movement-direction scores, diverse, flexor, and extensor, the subjects with the undetermined type emphasized flexor movement more than did the two other groups although all groups preferred extensor movement. Ideationally, subjects with the undetermined type emphasized animated objects or figures, animals, and inanimate objects; paranoid patients emphasized physiological, anatomical, and bodily processes, animals, and inanimate objects. Controls emphasized the human, animal, and botanical content.

Volitional movement of all objects was greater for controls, whereas disintegrative movement was greater for subjects with the undetermined type and for those with the paranoid type. In terms of all movement-level scores, female paranoid patients showed the most consistent sex-role reversals, performing more like male controls. Males and females with the undetermined type of schizophrenia showed equal sex-role reversals.

The three groups were successfully differentiated on the basis of the change-of-concept score: Controls were lowest, followed by patients with the undetermined type and by patients with paranoid schizophrenia. Paranoid women, in particular, were extremely high on this score. The change-of-concept score was related to sexual confusion and heightened environmental stimulation.

Anal contents were tremendously greater among paranoid subjects than among either of the two other groups. The projective-movement-sequence device elicits dynamic material at a level which appears deeper than that tapped by other projective methods. All groups respond with equal amounts of material for interpretation.

PHILADELPHIA NEUROLOGICAL SOCIETY

Michael Scott, M.D., *Presiding*

Regular Meeting, Nov. 2, 1951

Optic Atrophy Caused by an Arteriovenous Angioma: Report of a Case. LIEUTENANT RAYMOND I. BAND, Medical Corps, Army of the United States (by invitation).

The author presented a case of bilateral optic nerve atrophy and blindness of the left eye without other signs or symptoms. The cause, as determined at operation and by carotid angiography, was a vascular malformation in the supraclinoid region at the optic chiasm. This malformation could be included in the classification angioma racemosum, the aneurysma arteriovenosum of Bergstrand and Olivecrona. The literature was reviewed, and two somewhat similar cases were presented. No other case with optic nerve atrophy and blindness as the only presenting signs had been found in the literature.

DISCUSSION

DR. PAUL I. YAKOVLEV (by invitation): Was a bruit audible in this patient?

LIEUT. RAYMOND I. BAND, M.C., A.U.S.: No; I thought there was one when I first examined him, but this impression was not confirmed.

DR. PAUL I. YAKOVLEV: Do you then believe that an arteriovenous communication was actually present?

LIEUT. RAYMOND BAND, M.C., A.U.S.: We believed that the appearance of the lesion at operation with the arteriographic findings suggested this.

DR. GABRIEL SCHWARZ: Did you listen to the eyeball?

LIEUT. RAYMOND BAND, M.C., A.U.S.: Yes, we listened all over the skull and over both eyeballs. I thought at first that there was a bruit over the right internal carotid artery, but this could not be confirmed.

DR. RUDOLPH JAEGER: I believe it is rather unusual for a bruit to be heard unless an artery from outside the skull feeds the lesion. I believe that if all the vessels involved are entirely within the dura one does not hear any noise.

DR. N. S. SCHLEZINGER: This paper raises the whole question of vascular lesions in the region of the optic chiasm and the optic nerves. Obviously, such lesions should be diagnosed as early as possible. Visual fields are sometimes helpful, although they could not be used in this case because blindness had already developed. Air study and angiography are also helpful, and I agree that in this case the appearance of the chiasmatic cistern was suggestive. I should have suspected the presence of a neoplasm from that finding.

LIEUT. RAYMOND I. BAND, M.C., A.U.S.: That was also our opinion, and that is why arteriography was not performed until after the operation.

DR. ARNOLD LEVINE: Was headache prominent in this case?

LIEUT. RAYMOND I. BAND, M.C., A.U.S.: Only during the first month of the illness was any headache reported, and since he had been in combat it was difficult to evaluate this symptom. He has not had headache subsequently.

DR. MANUEL SALL: Were any skin nevi found?

LIEUT. RAYMOND I. BAND, M.C., A.U.S.: No. We found no other evidence of vascular abnormalities anywhere in the body.

Unusual Manifestations of Craniopharyngioma: Report of Five Cases. DR. JAMES A. L. MOULTON, Coatesville, Pa. (by invitation).

Five cases of craniopharyngioma with unusual manifestations were presented. Two of the patients were in the third decade of life; one, in the fifth, and two, in the sixth.

All five patients showed prominent psychiatric symptoms, ranging from a sensorial defect to mania. Three had evidence of pyramidal-tract damage, and two had endocrine changes. Other neurological manifestations included ocular muscle paralysis, optic nerve atrophy, ataxia, and convulsions. The duration of symptoms was approximately two years in the two patients for whom an adequate history was obtained.

All the tumors were cystic and occupied the interpeduncular space, extending into the third ventricle. One had a finger-like projection which passed over the right crus and ended as an embedded mass in the lateral aspect of the cerebellum, between the emerging fifth and eighth cranial nerves. Another extended caudally from the interpeduncular space to distort the left cerebral peduncle and the basis pontis. All five tumors compressed the hypothalamic structures and the optic chiasm. In three cases the foramina of Monro were occluded by tumor tissue causing dilatation of the lateral ventricles.

DISCUSSION

DR. JOSEPH YASHKIN: I should not have thought, from my own experience, that craniopharyngiomas constitute 4 to 5% of all brain tumors. The age of the patients in Dr. Moulton's series is certainly at variance with my clinical impression of this condition up to two or three years ago. I had always thought of children with this lesion as typically having large heads,

with visual disturbances and only questionable changes in the sella turcica, as seen with x-rays. In 20 to 25% calcification might appear above the sella. Some had papilledema and temporal cuts in the visual fields, but most of the children did not. In differential diagnosis, I should always think first of a craniopharyngioma, then of a meningioma, and finally of a tuberculoma. Lieutenant Band has called our attention to another possibility. It is true that the changes in the sella turcica are not pathognomonic. Exploration is always indicated for the preservation of eyesight, if at all possible. As has been pointed out, these tumors can certainly grow in any direction, and the more one knows about them, the more one realizes how confusing they can be.

DR. AXEL OLSEN: It is unfortunate that four of these five tumors were not found until autopsy. Even though often not much can be done about such tumors because of their infiltration, one does like to make the effort at least. I had a case of a 12-year-old girl in which the roentgenogram showed suprasellar calcification and in which I found no tumor or other lesion at operation. She has improved since the operation, and I cannot explain her condition. She may have had calcification as a result of toxoplasmosis, which we found produced calcification in an infant recently observed.

Even when the cyst is only drained, these patients have a 30 to 50% operative mortality. The solid portions of the cyst are highly adherent to surrounding structures. Short-circuiting of the spinal fluid by ventricular puncture may be palliative. It has also been suggested that the cyst be uncapped for drainage into the lateral ventricles, in the hope that it will not refill. On the whole, however, surgical results are not satisfactory.

DR. CHARLES RUPP: Was any calcification found in these cases, and was the condition recognized clinically, before death, in any of them?

DR. MICHAEL SCOTT: In what percentage of these cases were changes seen in the sella turcica?

DR. GABRIEL SCHWARZ: What do you think is the mechanism of symptom production with these tumors? Is it the result of pressure from the tumor itself or of invasion of such structures as the hypothalamus?

DR. JAMES A. L. MOULTON, Coatesville, Pa.: Calcification was observed in one case with x-rays but was not found post mortem. The diagnosis was made before death in two of the five cases. In both these cases the posterior fossa had been invaded by tumor tissue. Actually, roentgenograms were made in only two of the cases, and in both there were an enlarged sella and thinned clinoid processes.

DR. HELENA RIGGS: Actually, the craniopharyngioma does not invade surrounding structures deeply, but it is difficult to strip the tumor tissue from the surfaces; just as it is difficult to strip off an ependymoma. I was very much interested in the case in which acute internal hydrocephalus was obviously present but the patient had been dancing professionally only three or four days before her death.

Discography Combined with Ethyl Iodophenylundecylate (Pantopaque®) Myelography. DR. JEFFREY MOORE (by invitation), DR. VICTOR REYES (by invitation), and DR. HENRY WYCIS.

In an attempt to diagnose abnormalities of the intervertebral disk more accurately, Dr. Knute Lindblom, of Sweden, in 1941 injected disks with an opaque medium and has done this as a supplement to myelography for the past five years.

To evaluate the procedure, the authors studied a series of 28 cases at Temple University Hospital. Disk punctures were performed at the fourth-fifth lumbar and the fifth lumbar-first sacral levels. An 18-gauge spinal needle was inserted via the lumbar route into the subarachnoid space from a posterolateral direction. Through the lumen of this needle, a slightly larger, 22-gauge spinal needle was inserted and advanced until the tip of the smaller needle was in the disk zone. A small amount of 35% diodrast® solution was injected through the smaller needle, and film records were made. This injection often produces pain similar to the patient's chief complaint, and this sign is important.

Various patterns of dye distribution were found; they were described as perineural spread, degenerated-disk pattern, and protruded-disk pattern.

Routine myelograms were performed in as many of the cases as possible in this series, and results were compared with the operative findings.

In the authors' cases they had found disk puncture to be more accurate in the diagnosis of disk abnormalities than routine myelography (80%, as compared with 52.63%), but disk puncture does not exclude spinal-cord tumors; for this reason, they have not considered it a routine procedure.

DISCUSSION

Dr. Henry Wycis: Although discography originated in Sweden, I found this summer, when I visited Sweden, that it is not yet popular there. The Swedish surgeons use a dye similar to diodrast,® which is more irritating than ethyl iodophenylundecylate, but which outlines the root sheaths better and is absorbed rapidly. I believe that our paper is the first in this country to correlate myelograms with discograms, and it is my impression that discograms show fewer artifacts than myelograms, although it must be admitted that our series is a small one. I have thought that air has produced fewer artifacts than ethyl iodophenylundecylate, and I believe that the present method may show even less than air. There are real mechanical difficulties in performing this procedure, and it is remarkable that there were only two failures in this series. These results are better than those reported by Gardner and his associates, in Cleveland. While I do not believe that this procedure is necessarily the one of choice, it is deserving of more study.

Dr. Henry A. Shenkin: I am grateful for the discussion of this subject tonight, but I cannot see the indication for the procedure. The objections to myelography have been, first, that it is time-consuming; second, that it requires a good roentgenologist, and third, that it produces complications. The ideal procedure would be one in which the entire spinal canal is filled with a nonirritating contrast medium, and the discography not only fails to offset the disadvantages of myelography but reveals the condition in only one disk. It certainly would not rule out tumor. Is this procedure an effort on the part of roentgenologists to demonstrate a single lesion so clearly that they will not run the risk of reporting a lesion which is not demonstrable at operation?

Dr. Charles Rupp: Is there not real potential danger in this procedure? If one punctures a healthy disk and injects an irritating substance, is it not possible that the disk may rupture in six months or a year?

Dr. Joseph Yashkin: Did I understand Dr. Wycis to say that air myelography is better than the use of ethyl iodophenylundecylate?

Dr. Rudolph Jaeger: Diodrast ® is a very irritating substance, and I should hate to have it spilled into the subdural spaces. I believe that the procedure would be dangerous to a normal disk, since it could well start destructive processes. I believe that it should be demonstrated experimentally that this untoward effect cannot occur before the procedure is used clinically. I also am not sure that the findings would alter the clinical impressions significantly, since everyone is more and more inclined to depend on the clinical picture in deciding upon operation.

Major W. J. Kimsey, M.C., U.S.A. (by invitation): I should like to put in a plea for more freedom in operating with the local use of anesthesia. Our patients at Valley Forge Army Hospital tell us that these operations are not as uncomfortable even as myelography.

I also believe that the disk is vulnerable to damage by the procedure under discussion because it is avascular.

Dr. Joseph Yashkin: I feel that we should not regard these operations too lightly. They are not appendectomies. Certainly, neurologists see many patients who have been operated upon without very much success. Of course, I agree that there are patients who require operation, but I believe that many psychoneurotic persons are being operated on for this condition. Back pain and leg pain are now a fashionable form of conversion. It is also open to question whether a disk will be permanently disabling, since in the past we have not seen large numbers of people in hospitals with this condition as a source of chronic disability.

Dr. Rudolph Jaeger: I should like to take issue with Dr. Yashkin about the number of psychoneurotic persons who are operated on for this condition. Actually, I believe that in many cases in the past disks have continued to disable people and have given rise to considerable invalidism and drug addiction with morphine.

DR. HENRY WYCIS: Naturally, every new procedure is subject to attack, and I wish to make it clear that I do not advocate this procedure at this time. Dandy said, long ago, that myelograms were never really necessary for diagnosis, and I find in my own practice that I am doing less and less myelography. In answer to Dr. Yashkin's question, I meant only that air produces fewer artifacts than ethyl iodophenylundecylate—not that it is a better procedure. In answer to the question about performance of disk operations with the use of local anesthesia, I can only say that American patients generally will not tolerate it if they have any choice in the matter. In Norway I found that even craniotomies are done with local anesthesia, but we could not get away with this in America. I agree that there is some danger of spilling the diodrast,[9] but I should point out that this happened in only one case in our series. I also agree that there is a possibility of danger from the injection of a healthy disk, but I believe that this has not been demonstrated thus far.

Relation of Cerebral Circulation to Cerebrospinal Fluid Pressure: Clinical Considerations. DR. HENRY A. SHENKIN, DR. PAUL NOVACK (by invitation) and DR. BERNARD GOLUBOFF (by invitation).

The cerebral circulation was found to be greatly reduced in two cases of intracranial hypotension following the removal of a subdural hematoma. The reduced cerebral blood flow was caused by an increase in cerebrosvascular resistance, presumably due to a narrowing or spasm of the vascular channels of the brain. It is postulated that the reduced cerebral circulation was the cause of the intracranial hypotension and of the symptoms usually ascribed to the reduced cerebrospinal fluid pressure. This hypothesis was tested by measuring the spinal fluid pressure in a series of 10 patients before and during hyperventilation. Hyperventilation in each instance caused a lowering of the cerebrospinal fluid pressure, averaging 27%. On the contrary, administration of 5% carbon dioxide by inhalation caused an increase in spinal fluid pressure, averaging 65%. These observations show a definite correlation between the rate of cerebral blood flow and the pressure of the cerebrospinal fluid. It is further presumed that prolonged decrease in the cerebral blood flow in all probability leads to a reduced production of cerebrospinal fluid, and this, in turn, contributes to the intracranial hypotension. The treatment of intracranial hypotension should be directed to increasing the cerebral circulation, as by the administration of carbon-dioxide inhalations, rather than by attempting to restore cerebrospinal fluid pressure by intrathecal injection.

It does appear that the response of cerebrospinal fluid pressure to alterations in the carbon-dioxide tension of the blood varies in magnitude from patient to patient. Preliminary data in induced states of altered blood carbon-dioxide tension which correlate cerebrospinal fluid pressure, changes in cerebral blood flow and the clinical state of the patient seem to indicate that this procedure is a measure of the reactivity of the cerebral vessels. It is conceivable that merely recording the change in cerebrospinal fluid pressure with inhalation of carbon dioxide and hyperventilation, this being a measure of cerebrovascular reactivity, will permit differentiation of symptoms due to cerebrovascular disease from those due to parenchymal brain disease.

DISCUSSION

DR. MICHEAL SCOTT: How was carbon dioxide given? Did the application of the mask have anything to do with increasing venous pressure?

DR. GABRIEL SCHWARZ: Is lumbar-puncture pressure really a measure of intracranial pressure? Can hypotension intracranially really be recognized by measuring lumbar puncture pressure?

DR. MATTHEW MOORE: I recall that in 1938 I found that the flushing produced by nicotinic acid was accompanied by a rise in cerebrospinal fluid pressure.

DR. RUDOLPH JAEGER: Is there any correlation between the systemic blood pressure and the cerebrospinal fluid pressure? I should think there would be.

DR. HENRY WYCIS: Dr. Spiegel and I found, in our experimental work, that it was always difficult to make allowance for variations in the systemic blood pressure.

DR. AXEL OLSEN: Was papaverine used with any of these patients?

DR. HENRY A. SHENKIN: The effect of the masks on these patients was carefully controlled, and we found that in itself the mask had no effect on the cerebrospinal fluid pressure. Obviously, if there is a block between the intracranial spaces and the lumbar region, the lumbar pressure will not be an accurate measure. There was no such block in any of these patients. With regard to nicotinic acid, it has been demonstrated that its effect is most pronounced on extracranial vessels, rather than on intracranial blood flow. Blood pressure was recorded continuously by means of a cannula in the femoral artery in all these patients. There was no correlation with the arterial pressure. Actually, intrinsic factors, such as resistance of the intracranial vessels, make the effect of increased systemic blood pressure of little importance intracranially. We did not use papaverine in the study of any of these patients.

PHILADELPHIA NEUROLOGICAL SOCIETY AND NEW YORK NEUROLOGICAL SOCIETY

Calvin S. Drayer, M.D., and Harold Wolff, M.D., *Presiding*

Joint Meeting, April 18, 1952

Motor Disorders in Nervous Diseases of the Dog (with Motion-Picture Demonstration). DR. JOHN MCGRATH, New York (by invitation), and DR. HELENA E. RIGGS, Philadelphia.

A moving picture was shown depicting various neurological disturbances in dogs. The picture is divided into two basic parts.

1. Spinal-cord Disturbances: This part included cases of spinal neoplasm, focal epidural pachymeningitis with contusion of the cord, diffuse ossifying pachymeningitis, encephalomyelitis with dominant cord symptoms, and bilateral paralysis of the foreleg due to contusion of the cord.

2. Brain Disturbances: This part included cases of encephalitis with various neurological symptoms, such as disorders of gait and coordination, circling, tic or tremor, and abnormal reflexes, and cases of brain tumors, illustrating localizing signs and a convulsive seizure.

DISCUSSION

DR. HAROLD G. WOLFF, New York: Stockard, at Cornell, mated healthy pedigreed St. Bernard and Great Dane dogs and found that in a high percentage of offspring paresis of the hindlegs developed at the age of 8 to 14 weeks. The animals killed then showed dying anterior horn cells and lateral column cells. In the animals killed later loss of such cells was detected only by comparative counts. Besides paresis of the hindlegs, these dogs exhibited persistent priapism, attributed to death of autonomic cells in the lumbar region. Stockard suggested a relation of these phenomena to the Werdnig-Hoffmann syndrome (hereditary familial spinal muscular atrophy) seen in humans. The carefully studied accidents of nature presented by the authors represent a step toward better understanding of human problems.

DR. JOHN R. WHITTIER, New York: Motion-picture demonstration began with interest in animal movement. Eadweard Muybridge, late in the 19th century, devised the "zoopraxoscope" to determine whether horses' feet all left the ground at once, and the physiologist Marie, about 1894, used the method as a research tool to study righting reactions in cats. Dr. Wolff noted the extensive material available for neurological experiment in naturally occurring animal diseases, such as were shown here. A large pharmaceutical house is currently using post-encephalomyelitic spasms in dogs for the evaluation of new drugs, and in our own laboratory my colleagues and I are using such specimens in cinematographic studies of dyskinesia.

DR. S. PHILIP GOODHART, New York: For interpretation of the complex pictures presented by Dr. McGrath, I would urge the use of slow-motion cinematography.

In studying the dyskinesias in man, I have found that slow-motion photography often revealed the presence of abnormal motor expression which was neither apparent to the naked eye nor demonstrable by the applied hand. Twelve years ago, at a meeting of the American Neurological Association in Atlantic City, the late Dr. Frederick Tilney and I demonstrated such a dyskinesia in a case of dystonia musculorum which we presented by motion picture projected in slow motion. We called the phenomenon a "vermiform" type of muscle dyskinesia. We regarded it as a clinical expression of a lesion in the corpus striatum.

Surgical Treatment of Spasmodic Torticollis. Dr. Henry T. Wycis, Philadelphia.

This presentation was essentially a motion-picture demonstration of the surgical treatment and its results in seven cases of spasmodic torticollis. The operation consisted in the intradural section of both spinal accessory nerves and the anterior roots of the first three cervical segments. In Case 5 the anterior roots of the first four cervical segments were sectioned. Cases 2, 3, 4, 5, and 6 were presented cinematographically. In six cases there was marked improvement; in one, Case 7, partial improvement. In all but one case (Case 4) the patient had the benefit of psychiatric treatment. There were no deaths.

DISCUSSION

Dr. Fritz J. Cramer, New York: Spasmodic torticollis is a symptom, not a disease entity. Its pathogenicity is as diverse as its clinical manifestations. When it is organic in origin and resistant to psychotherapy, good surgical results are obtained only in the type with localized rapid severe movements. Progressive, dystonic spastic forms do poorly. Dr. Wycis' uncommonly excellent results reflect proper selection of cases and appropriate surgical procedure. For example, in the case in which the first four cervical roots were cut because the movements were clearly beyond the scope of the first three cervical roots alone, a perfect result was obtained.

Dr. Edward Schlesinger, New York: From a brief review of our cases at the New York Neurological Institute, I should say our failures were due, first of all, to technical faults and, second, to anatomical variations. A third group were the cases in which the torticollis later went on to generalized dystonia. In this group the operation not only proved to be valueless but increased the severity of the patient's symptoms complex and added pain.

The operation is one of deprivation, and one would like to think of a more physiological approach. Dr. Merritt once said that if we understood what happens during sleep, we could solve these vexing problems.

Since torticollis seems so intimately related to postural mechanisms, it is too bad we have not been more concerned with its relation to disorders of reflex posture.

I am struck by the lack of disability shown in the cases presented here, and I wonder especially about normal diaphragmatic function in the patients with section of the first, second, third, and fourth cervical roots.

Dr. Henry T. Wycis, Philadelphia: I do not believe that one cures spasmodic torticollis with this operation, and had I operated on every patient with so-called spasmodic torticollis I had seen I am sure the results would have been far from what you have seen.

That brings up a point of case selection. One must carefully select patients by analyzing the extent of their movements.

With regard to the pathology, Dr. Cramer was under the impression that the pathologic process was in the region of the basal ganglia. This was likewise Foerster's opinion. He believed that torticollis was always organic. I believe there is a psychogenic component in many cases, but whether or not that is the etiological factor is questionable.

With regard to the pain that Dr. Schlesinger mentioned, it should be noted that all these operations were done with the posterior roots spared. Nevertheless, the patient has pain after operation for a short time because there is some stretching of the posterior roots in getting at the anterior roots.

Regarding the innervation of the diaphragm, I must admit that it was with some fear and trepidation that I sectioned both the fourth cervical roots anteriorly. The diaphragm was not involved, apparently, since it is supplied by the third, fourth, and fifth cervical roots. If I had been dealing with a prefixed brachial plexus, I might have had a fatality. Sparing of the fifth cervical root was apparently sufficient to allow the diaphragm to function.

Acute Poliomyelitis: Differential Diagnosis of 409 Devised Diagnoses. Dr. Anthony S. Tornay, Dr. Alexander Silverstein, Dr. Katherine E. Dawson (by invitation), and Dr. Alfred La Boccetta (by invitation), Philadelphia.

In the 10 years from 1940 to 1949, inclusive, 1,420 patients were admitted to the poliomyelitis wards of the Philadelphia Hospital for Contagious Diseases. The diagnosis was confirmed in 1,011 patients, and in 409 patients (28.9%) it was revised after clinical and laboratory evaluation.

Of these 409 patients, 113 were found to have other organic disease of the central nervous system; 8 had a disturbance of the peripheral nervous system; 13 apparently suffered from a psychogenic disorder; 114 had a disorder diagnosed as respiratory infection; 77 had a disturbance diagnosed as musculoskeletal disease; 17 had gastrointestinal disease; 18 had genitourinary disease; 5, acute febrile illnesses, and 10, diseases of the skin and allied structures.

It is gratifying to see that our revised diagnoses compared favorably with reports by other authors. It was also gratifying to note that 28% of the patients with revised diagnoses had other disease of the central nervous system and 28% had an acute infection of the respiratory tract, which frequently goes hand in hand with poliomyelitis. We were surprised at the large number of patients (27) with acute rheumatic fever. For 17 patients no diagnosis was made.

This study clearly demonstrates the need for close cooperation of the departments of neurology, pediatrics, and internal medicine of the hospital caring for patients with acute poliomyelitis.

DISCUSSION

DR. FRED PLUM, New York: The significance of these data depends on who made the presumptive diagnosis of poliomyelitis. It appears that the recognition of poliomyelitis has been so emphasized that basic principles of diagnostic reasoning have been rejected in an effort not to miss a disease of which so many are apprehensive. The danger is demonstrated by the figures: One fourth of the patients had serious and largely dissimilar illnesses, which if not treated specifically and promptly could result in disability or death. If such errors are to be prevented, broader programs of medical education must counterbalance the disproportionate attention that fund-raising organizations give to individual diseases which represent but a small part of the community health program.

DR. FLETCHER H. MCDOWELL, New York: Limitation of the criteria for diagnosis of anterior poliomyelitis to lower-motor-neuron paralysis, pleocytosis, and fever makes the diagnosis of poliomyelitis fairly certain. At present, in the absence of any specific therapeutic measure for the treatment of poliomyelitis, there is no great advantage in making the diagnostic criteria so general as to lead to confusion. This paper does point out the great number of diagnostic possibilities which can be confused with poliomyelitis, and which must be considered when specific treatment is available and treatment in the nonparalytic stage becomes a necessity. At present lumbar puncture is by far the most valuable laboratory procedure in making a diagnosis of poliomyelitis; if carried out, it will exclude most of the confusing diagnostic possibilities mentioned by Dr. Tornay.

DR ANTHONY S. TORNAY, Philadelphia: There are several ways in which patients come to the municipal hospital—in Philadelphia we call it the Hospital for Contagious Diseases.

First, we receive patients from other hospitals. These patients may have been admitted only to the receiving ward of another hospital and then have been sent to the municipal hospital, or the patient may have been in the hospital and then have been transferred to the municipal hospital as having poliomyelitis, for it is the custom of the city of Philadelphia to have a central treating station—the two are the Hospital for Contagious Diseases and the Children's Hospital.

Second, a practicing physician may call up the hospital and request admission. If the superintendent of the hospital knows the physician, he may admit the patient directly from the physician, or he may send out a physician from the Department of Public Health to examine the patient.

Third, we receive word from a physician or a hospital that a patient outside the city of Philadelphia belongs to the city, is a resident, and has poliomyelitis. The patient is therefore sent by ambulance to the hospital.

These are the methods of admission. There is no clinic at the hospital to which the patient may go to be examined for direct admission. This, therefore, brings out the impossibility of discussing Dr. McDowell's question. We have no idea how many patients have had spinal punctures prior to admission to the hospital.

Meningioma of the Tuberculum Sellae. DR. FRANCIS C. GRANT, Philadelphia.

A meningioma of the tuberculum sellae may give as few indications of it presence as any lesion with which the neurosurgeon has to deal. If this tumor is to be treated successfully

and safely, the decision to operate must be based on two symptoms alone: a defect in the temporal field and mild optic nerve atrophy.

The results of the surgical attack on a tumor in this position in a series of 27 cases were reported. The importance of early diagnosis was stressed. Symptoms were monotonously uniform—always visual loss in one eye, slowly developing blindness in that eye, and diminution of acuity in the opposite temporal field. Eighteen of the patients were entirely blind, or had light perception only in one eye when the diagnosis of tumor was finally made.

Of these 27 tumors, complete removal was accomplished of only 11. In seven of these cases the sella appeared normal in x-ray studies. In no instance in this series in which the sella was sufficiently distorted to make the localization of the tumor obvious from this evidence alone was total extirpation considered safe. Partial removal was carried out in 16 cases. There were eight fatalities.

DISCUSSION

DR. J. LAWRENCE POOL, New York: Our cases at the Neurological Institute also point up difficulties in early diagnosis: Plain roentgenograms of the skull may show no abnormality; anosmia is infrequent, and a history of "sudden" blindness in one eye may lead to a diagnosis of multiple sclerosis. The most reliable diagnostic aid is measurement of the visual fields, often neglected until too late.

Angiography is of great value in differential diagnosis and in planning craniotomy. Resection of some frontal cortex is necessary for successful removal of large tumors and reduces postoperative complications. Planned hypotension materially aids removal of the more vascular tumors.

DR. PETER DENKER, Philadelphia: What, roughly, was the age group in this study? As I understand it, age should be a helpful means of differentiation. Were most of the patients over 45 or 50?

DR. FRANCIS C. GRANT, Philadelphia: I am very much obliged to Dr. Pool for coming here to discuss these cases. I think it is true that the neurologist and neurosurgeon, as a rule, are not to blame for the late diagnosis. It is the ophthalmologist.

I talked to the ophthalmologists last night on this subject, trying to impress on them that a slow, progressive loss of the temporal field in one eye with optic atrophy does not necessarily mean a sinus infection; rather, before it is too late, one must think of the possibility of a tumor of this kind, and by angiography or by air encephalography the diagnosis can reasonably and readily be made.

Our average age was 39 plus, which is a lower age limit than usual, probably due to the inclusion of two children of 7 and 13. The age at which this tumor most frequently occurs is probably 35 to 45.

A Tumor of the Optic Disk Associated with Neurofibromatosis. DR. ROBERT H. TRUEMAN and DR. I. EDWARD RUBIN, Philadelphia.

A tumor of the right optic disk, occurring in a white man aged 32 and associated with neurofibromatosis (Recklinghausen's disease), was reported. The diagnosis of neurofibromatosis had first been made nine years previously by microscopic examination of biopsy nodules from the chest wall and the discovery of café au lait spots. Later pain developed in the left shoulder and arm. After investigation, a cervical laminectomy was done in September, 1948, at which time four small tumors were removed; these proved to be neurofibromas. A second laminectomy was done in June, 1949, but no tumors were found, although a diagnosis of postoperative syringomyelia was made.

Ophthalmologic examination, in 1951, revealed a tumor of the right optic disk. It is interesting to note that at the age of 16 a tentative diagnosis of tumor of the optic nerve head was made at Wills Hospital, but the investigations were never completed, owing to lack of cooperation of the patient.

Roentgenograms of the chest at the Philadelphia General Hospital revealed densities in both apices which were considered to be neurofibromatous in origin.

The patient had a suggestive family history in that his mother was stated to have nodules of the skin, and one sister had what from the description are café au lait spots.

The authors discussed the rarity of tumors of the optic disk in association with neurofibromatosis, and gave a short description of the two previously reported cases, the first by Stallard, in 1938, and the second by Goldsmith, in 1949, with a comparison of all three cases. The question of the occurrence of optic-nerve tumors in association with neurofibromatosis was discussed, with the various theories concerning the relation of the two conditions.

DISCUSSION

DR. H. HOUSTON MERRITT, New York: Dr. Trueman and Dr. Rubin have presented a thorough review of the ocular complications of Recklinghausen's disease. The case they present is unique in that the tumor involved the nerve head. As they pointed out, tumors of the optic nerve in patients with neurofibromatosis are not uncommon, but it is extremely rare for a tumor to originate at the distal end of the optic nerve and actually to involve the optic disk. They were able to find only two cases in the literature, and they have added one case.

It is well known that in neurofibromatosis many different types of tumors may occur and tumors within the parenchyma of the nervous system are not uncommon. Dr. B. E. Sprofkin reviewed the cases at the Neurological Institute of New York for the incidence of glioma of the optic nerve and neurofibromatosis. He found 19 cases of glioma of the optic nerve, but in only 1 of these was the tumor associated with neurofibromatosis. In one case the patient had a relative with a history suggesting neurofibromatosis.

Only four cases of neurofibromatosis had been studied at necropsy. Tumors of the central nervous system were found in all four cases but there was no instance of glioma of the optic nerve. In one case there was gliosis of the optic nerve which was suggestive of an early, but not fully developed, glial tumor. In all four cases of neurofibromatosis tumors occurred elsewhere in the central nervous system. In the first one there was meningiomatosis of the cerebral dura; in the second, an astrocytoma of the cerebrum; in the third, a meningioma and an astrocytoma, and in the fourth, a ganglioneuroma, together with some enlargement of several of the cranial nerves.

Since neurofibromatosis is accompanied by tumor formation and the tumor need not be a fibroma—in fact, it not infrequently is a meningioma—it is not surprising that occasionally a glioma of the optic nerve is associated with neurofibromatosis. The unique thing about the case presented here, of course, is the involvement of the nerve head.

DR. HAROLD WOLFF, New York: I understand that Dr. Gilpin has seen this patient. Has he any comment?

DR. SHERMAN F. GILPIN JR., Philadelphia: I examined him, and in my opinion his present clinical condition is that of syringomyelia. He has atrophy and lower-motor-neuron disease, and the other signs that go with syringomyelia. These signs apparently developed after the last laminectomy.

DR. HAROLD WOLFF, New York: Has Dr. Helena Riggs had any experience with this type of tumor?

DR. HELENA RIGGS, Philadelphia: In the one case I reported at the previous meeting with the New York Society a meningioma infiltrated or invaded the dural sheet, cupped around the back of the globe, and did not involve the nerve head directly.

DR. GEORGE GAMMON, Philadelphia: I am sure students of this disease are aware of the the fact that it is common in red snappers.

Dr. Lukay, in our Pathology department, has studied this tumor and has directed attention to the fact that since this species inhabits the waters of the Gulf Stream around the Keys in great profusion around the winter months, it might provide an excellent opportunity for you to pursue the question of the involvement of the optic nerves.

DR. ROBERT H. TRUEMAN: I should like to comment that syringomyelia has been reported as occurring in coincidence with neurofibromatosis.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Physiology and Biochemistry

EFFECT OF LOW FAT AND HIGH FAT DIETS ON THE SYNTHESIS OF CHOLESTEROL IN RATS. R. B. ALFIN-SLATER, M. C. SCHOTZ, F. SHIMODA and H. J. DEUEL JR., J. Biol. Chem. **195**:311, 1952.

The amount of cholesterol synthesized by the liver and appearing in the plasma under various experimental dietary conditions has been determined by the measurement of the uptake of deuterium into the cholesterol at the end of definite time intervals. It has been found that the amount of newly formed cholesterol present in the liver and plasma of rats prefed a low-fat diet is unchanged when the animals are placed on a high-fat diet. In the livers of the animals prefed a high-cholesterol diet synthesis was fairly depressed at the end of 8 days on the low-fat diet; at the end of 16 days synthesis had returned to normal. However, in animals on the high-fat diets synthesis of cholesterol in the liver was normal at the end of eight days. The newly formed cholesterol appearing in the plasma of rats prefed a high-cholesterol diet is much lower than that found in the control animals. A possible explanation of this difference has been postulated. A high-fat diet seems to be more efficient in removing the cholesterol which had accumulated in the liver during the preexperimental cholesterol feeding.

PAGE, Cleveland.

DEFECTS IN REGULATORY MECHANISMS OF AUTONOMIC FUNCTION IN INJURIES TO SPINAL CORD. L. J. POLLOCK, B. BOSHES, H. CHOR, I. FINKELMAN, A. J. ARIEFF, and M. BROWN, J. Neurophysiol. **14**:85 (March) 1951.

By observations on many patients with severe injuries to the spinal cord who survived World War II, it has been possible to compare the residual effects of such injuries with the effects of acute injury reported after World War I.

The authors show that, just as in the case of skeletal muscle supplied by spinal motor efferent fibers, so in the case of sweat and other glands, of smooth muscle, and of blood vessels uninnervated by the sympathetic outflow, the resultant defects in function are the same when the spinal cord is severely injured or transected.

On the one hand, the interruption of central excitatory, or suprasegmental, impulses for heat production, sweating, and vasoconstriction produces defects in regulation of sweating, heat production, and blood pressure. Central inhibitory impulses leading to diminished chemical heat production, when interrupted, result in increase over normal hyperpyrexia as the result of immersion in hot water. On the other hand, interruption of inhibitory impulses from suprasegmental levels results in excessive reflex hypertension and sweating.

ALPERS, Philadelphia.

CHANGES IN EXCITABILITY OF CEREBRAL CORTEX FOLLOWING SINGLE ELECTRIC SHOCK APPLIED TO CORTICAL SURFACE. H. CHANG, J. Neurophysiol. **14**:96 (March) 1951.

The excitability of cortical neurons was studied by means of local cortical potentials elicited either by a single electric shock stimulus applied to the cortical surface or by afferent stimulation. Consequent to a single electric shock stimulus the cortical neurons underwent a period of refractoriness, followed by a prolonged secondary depression. The degree and duration of the secondary depression varied with the strength of the stimulus and the number of cortical neurons previously activated by the conditioning shock. The severest depression was observed in the cortex locally treated with strychnine.

In the auditory cortex of the cat a single electric shock stimulus produced a periodic variation of cortical excitability with a frequency coincidental with that of the corticothalamic reverberating waves. The excitability was increased during the developing phase of the reverberating waves and decreased during the returning phase. The phase relations of the reverberating waves and the fluctuations of the excitability curve of cortex can be expressed mathematically.

Chang suggests that the processes of the change in excitability of cerebral cortex following stimulation with a single shock are analogous in basic principles to the change in excitability of spinal motor neurons or that of peripheral nerves.

ALPERS, Philadelphia.

ASCENDING CONDUCTION IN RETICULAR ACTIVATING SYSTEM, WITH SPECIAL REFERENCE TO THE DIENCEPHALON. T. E. STARZL, C. W. TAYLOR, and H. W. MAGOUN, J. Neurophysiol. **14**:461 (Nov.) 1951.

Recent study has revealed a cephalically directed brain-stem system stimulation of which desynchronizes the electrical activity of the cerebral cortex in a manner simulating that observed in awakening from sleep or in the electroencephalographic arousal reaction. This system was found to be distributed in the reticular formation of the medulla, the tegmentum of the pons and midbrain, and the subthalamus and hypothalamus. The means by which its activating influence became exerted on the cortex was speculated upon. Because of the generalized distribution of the cortical effects, it seemed likely that the diffuse thalamic projection system was concerned.

In the present study the ascending course of the reticular activating system was investigated in the brain stem of the cat, with special reference to conduction through the diencephalon.

With repetitive stimulation of this system in the bulb or midbrain, desynchronization of electrical activity was observed in the subthalamus and hypothalamus, the ventromedial part of the thalamus, and the internal capsule. Potentials evoked by single-shock reticular stimuli were recorded from the same areas. Excitation of these diencephalic regions, in turn, induced generalized desynchronization of electrocortical activity, and single-shock stimuli delivered to them evoked widely distributed cortical potentials.

These results suggest that alternative routes are available for corticipetal conduction of the reticular activating influence over (1) a thalamic path involving transmission to the ventromedial part of the thalamus, with relays to the cortex from the remainder of this structure, and (2) an extrathalamic path involving direct passage into the internal capsule from the subthalamus and hypothalamus. In agreement, after selective destruction of either of these routes, leaving the other intact, generalized desynchronization of electrocortical activity could still be elicited by stimulation of the lower part of the brain stem.

ALPERS, Philadelphia.

ON CERTAIN ASPECTS OF THE SENSORY ORGANIZATION OF THE HUMAN BRAIN: II. A STUDY OF ROSTRAL DOMINANCE IN CHILDREN. R. COHN, Neurology **1**:119 (March-April) 1951.

Approximately 50 essentially normal children between the ages of 3 and 10 years were examined for evidence of rostral dominance. The subjects were normal with respect to their sensory apparatus as determined by responses to disparate single cutaneous stimuli. The remarkable finding was that nearly all the children between the ages of 3 and 5½ years showed persistent patterns of response which in all ways resembled the picture observed in adults with irreversibly disturbed brain-cell activity. At the critical age of approximately 6 years in the grossly normal child, the pattern of rostral, or proximal, dominance is no longer evident, or it is evoked (as in the normal adult) in the first or second pair of stimulation. Persistence of the phenomenon of rostral dominance in a well-developed child past the age of 6 years has proved to be fair evidence of mental retardation.

From these results it is obvious that there is an innate pattern of perception of multiple simultaneously applied ipsilateral cutaneous stimuli. When the phenomenon is observed in the adult as part of a disease process, it represents a regression to a more primitive level of perception and adaptation. Moreover, these results indicate that sentiency of, and the resolution of, multiple disparate stimuli is a learned process, and that the apparatus necessary for this learning develops, and is utilizable for this purpose, at the approximate age of 6 years in the normal child.

ALPERS, Philadelphia.

STUDIES ON THE PHYSIOLOGY OF AWARENESS: ANOXIA AND THE LEVELS OF SLEEP. J. W. LOVETT DOUST and R. A. SCHNEIDER, Brit. M. J. **1**:449 (March 1) 1952.

Lovett Doust and Schneider made a study of the sleeping habits and levels of sleep of seven normal, healthy subjects. Photoelectric oximetry in a series of 22 observations on these subjects suggested the following planes of sleep: (1) wakefulness (arterial oxygen saturation,

96%); (2) presleep (90 to 92%); (3) light sleep (89 to 91%); (4) deep sleep (87 to 88%); (5) light sleep following deep sleep (89 to 91%); (6) prewakefulness (90 to 92%), and (7) awakening (92 to 98%).

There was a differential correlation of muscular movements, posture, scratching, respiratory adjustments, and responses to external stimuli with all these separate planes.

The various physiologic concomitants of sleep closely resembled those accompanying states of anoxemia.

Lovett Doust and Schneider suggest that the concepts of homeostasis and dynamic psychology, psychiatry, and maturation bear an important relation to the phenomena of fluctuating awareness, anoxia, and sleep.

ECHOLS, New Orleans.

SOME PROPERTIES OF ISOLATED CEREBRAL CORTEX IN THE UNANAESTHETIZED CAT. B. DELISLE BURNS, J. Physiol. **112**:156-175 (Jan.) 1951.

A slab of cerebral cortex from the suprasylvian gyrus of the cat, 20 by 6 mm. and 7 mm. thick, was prepared in such a way that it was isolated from the animal except through its blood supply. Such a preparation exhibits no spontaneous activity after the temporary discharges due to operative injury have subsided. A single electrical stimulus gave rise to two types of response: a local, short-lasting, surface-negative response, and a prolonged, surface-positive response, which spread without attenuation to the borders of the isolated area. The surface-negative response did not differ from that obtained in anesthetized animals with intact cortex. Evidence is provided that the surface-positive response is transmitted in a single, deep-lying layer of cells interconnected in all directions through dendrites and synapses. It is concluded that their repetitive response is the consequence of self-reexcitation in closed chains of neurons. The average circumference of the neuron ring around which excitation circles is estimated at about 2 mm. The irritability of its layer responsible for the surface-positive response was reversibly reduced by anesthetics and anoxia; this response was abolished by full surgical anesthesia, which did not affect the surface-negative response.

THOMAS, Philadelphia.

A FURTHER SURVEY OF THE ACTION OF CLOSTRIDIUM BOTULINUM TOXIN UPON DIFFERENT TYPES OF AUTONOMIC NERVE FIBRE. N. AMBACHE, J. Physiol. **113**:1-17 (March) 1951.

The author investigated the susceptibility of various types of nerve fibers to the paralytic action of botulinum toxin. Of the nerve fibers tested, all preganglionic fibers and all postganglionic cholinergic fibers were paralyzed. The preganglionic fibers tested were the fibers to the ciliary ganglion and the superior cervical ganglion. Postganglionic cholinergic fibers included sudomotor fibers and short ciliary nerves. Adrenergic fibers, e. g., the pupillodilator fibers, were unaffected by doses 200 to 300 times as large as those which caused paralysis in cholinergic fibers. The authors conclude that cholinergic fibers are susceptible whether they are preganglionic or postganglionic, and whether they belong to the sympathetic or to the parasympathetic system.

THOMAS, Philadelphia.

ABNORMAL WATER METABOLISM IN SIMMONDS' DISEASE. J. DOUGLAS ROBERTSON, Lancet **2**:282 (Aug. 18) 1951.

For many years it has been recognized that in cases of Addison's disease there is no diuresis after large intakes of water. A similar picture was noted in Simmonds' disease, a syndrome somewhat resembling Addison's disease. In both conditions there is adrenocortical insufficiency; this is a primary symptom in Addison's disease, whereas in Simmonds' disease it is secondary to a lack of one or more adrenocorticotropic hormones.

Robertson studied a case of Simmonds' disease to find an explanation for the abnormal water metabolism. Two observations pointed to a possible answer: 1. The night urine almost invariably exceeded the day output, instead of there being a normal 3:1 ratio in favor of the day urine. 2. When the water test of Robinson and co-workers was made from 9 p.m. to 1 a.m., instead of from 9 a. m. to 1 p. m., there was a greater excretion of urine. This suggested that in Simmonds' disease increased diuresis might take place during the night. It is suggested that a possible cause of the failure to obtain increased diuresis after large intakes of water is an

antidiuretic substance probably elaborated by the posterior lobe of the pituitary that is present during the day but absent during sleep. It also explains the failure to obtain concentrated urine in the morning under standard conditions when it can be obtained from normal people.

Corticotropin, cortisone, and implants of desoxycorticosterone and testosterone propionate, with thyroid by mouth, did not alter the specific changes found in the water metabolism of Simmonds' disease.

MADOW, Philadelphia.

Neuropathology

EPENDYMOMA: A CRITICAL RE-EVALUATION OF CLASSIFICATION WITH REPORT OF CASES. C. E. TROLAND, J. F. KENDRICK, P. F. SAHYOUN, and F. B. MANDEVILLE, J. Neuropath. & Exper. Neurol. **10**:295 (July) 1951.

Because the ependymal cell is the earliest to differentiate from the neural tube, Troland and his colleagues were of the opinion that a critical study of the ependymal tumors as a group, regardless of where they arise, should facilitate the comprehension of tumors of the nervous system.

An embryologic review reveals four important points: 1. Chronologically, the ependymal cell is the earliest to assume its identity. 2. Morphologically, the ependymal cell is the only cell of the nervous system which retains its epithelial characteristics, i. e., of a lining or covering cell. 3. The distribution of the ependymal cells is also typical, for they line the ventricles of the brain and the central canal of the spinal cord and are found in the filum terminale. 4. The structures which are closely related to the ependymal cells are the germinal cells, which ultimately give rise to the neuroblasts and the primitive spongioblasts, the forerunners of the nerve, glia, and pineal cells.

The widespread distribution of ependymal tumors is striking. No less significant is the multiformity of the cell patterns in different tumors, as well as in different areas of the same tumor.

A critical reevaluation of the classification of ependymomas implies a retrograde scale, which should parallel the grade of malignancy.

Grade 1, indicating the lowest grade of malignancy, includes the three well-recognized groups, namely: (1) papilloma choroidium; (2) myxopapillary ependymoma; (3) epithelial ependymoma.

Grade 2 includes the cellular forms, which continue to show the ependymal linkage.

Grade 3 includes some of the malignant forms of ependymoma, where, with the papillary and epithelial structures, there are found syncytial areas, mitotic figures, or oligodendroglia-like cells. In other words, Grade 3 illustrates a retrogression or dedifferentiation of the cell to the stage before or about the period when the oligodendroglia is differentiated, and the tumor attempts to mimic this phase.

Grade 4, representing a very anaplastic growth, duplicates closely the cellular make-up of the mantle layer. These tumors contain primitive neuroepithelial cells, spongioblasts, primitive pineal cells, and the so-called medulloblasts.

The anaplastic form or Grade IV of any type of brain cell is essentially a duplicate of the multipotent syncytium-like "mantle layer" cell. Mantle is derived from the Latin "mantellum," and these workers feel that to designate a tumor in this group as "mantellomas" would bring to mind the development and origin of the nervous system, and lead toward a better comprehension of tumors of the nervous system.

ALPERS, Philadelphia.

Meninges and Blood Vessels

GRANULOMATOUS ENCEPHALOMYELITIS IN INFANCY. J. P. WYATT and W. W. TRIBBY, A. M. A. Arch. Path. **53**:103 (Feb.) 1952.

The genesis, morphological aspects, and fate of inflammatory lesions occurring in the central nervous system of infants have been clouded for years by Virchow's concept of congenital interstitial encephalitis. Although in rare instances agents of a viral, fungal, or metallic nature have been labeled as producing fatal encephalomyelitides, it is only within the last 10 years that infection, particularly that due to toxoplasma, has been recognized as a dominant agency in the production of infantile encephalomyelitis.

Wyatt and Tribby report six cases of granulomatous encephalomyelitis in infants. In two cases the cause was toxoplasmic and in one the intracranial lesions were produced by the salivary-gland virus. In the remaining three cases the morphological evidence strongly suggested an infectious origin. In the six cases the duration of illness varied from 16 days to 8 months. The clinical manifestations were protean, and in several cases the ultimate sequelae were hydrocephalus, porencephalic healing, extensive gliosis, and change of vascular pattern.

This study supports the view that some cases of brain deformities previously believed to be genetic may in reality represent the end-results of infectious mutilation.

WINKELMAN, Philadelphia.

MYCOSIS OF CERVICAL SPINAL CORD FOLLOWING INTRATHECAL PENICILLIN THERAPY. ROBERT E. WYBEL, A. M. A. Arch. Path. **53**:167 (Feb.) 1952.

Wybel reports a fatal case of mycotic granuloma involving the leptomeninges of the cervical portion of the spinal cord, probably due to Aspergillus. The identification of the infecting agent in this case was difficult because the body had been embalmed and cultures, therefore, were not taken at autopsy. A study of the fungi in the tissue sections revealed both hyphae and spores; on this basis, all pathogenic fungi except Candida (Monilia), Aspergillus, and Mucor could be eliminated from consideration. The large, irregular, nonseptate, branching hyphae characteristic of Mucor were not observed. The distinction between Candida and Aspergillus was more difficult. However, the organism was probably Aspergillus, as indicated by the relatively large size of the hyphae, their prominent lateral branching and the small number of spores.

The meninges of the cervical portion of the cord were the only site of mycotic involvement. The clinical course and the histologic appearance of the granuloma suggest a long-standing, chronic lesion, compatible with origin at the time of the patient's illness with pneumococcic meningitis. The aspergilli are described as "weeds of the culture room" and are common laboratory contaminants. In the case reported it is possible that they were introduced into the subarachnoid space during lumbar puncture as contaminants from the skin or the needle. The fungi may even have been present in the penicillin solution injected intrathecally three years prior to death, during treatment of the pneumococcic meningitis. Evidence is cited from the literature indicating that the growth of the fungus was increased by the penicillin therapy. This complication should be added to the long list of dangers associated with the intrathecal administration of penicillin and other antibiotics.

WINKELMAN, Philadelphia.

ARTERIOGRAPHIC DEMONSTRATION OF SPASM OF THE INTRACRANIAL ARTERIES, WITH SPECIAL REFERENCE TO SACCULAR ARTERIAL ANEURYSMS. A. ECKER and P. A. RIEMENSCHNEIDER, J. Neurosurg. **8**:660 (Nov.) 1951.

The percutaneous method of puncturing the carotid artery allows the repeated performance of cerebral angiography on the same patient. The cerebral arteries thus visualized with the same technique on different occasions generally are identical but sometimes differ strikingly in caliber. When the artery has the smaller caliber, it is said to be in arterial spasm. In this paper the authors present their observations on such spasm and discuss its possible significance.

Spasm of the larger intracranial arteries (internal diameter at least 1.5 mm.) was demonstrated in 12 instances among 10 cases by means of comparative arteriograms. The affected vessels were the internal carotid, anterior cerebral, and middle cerebral arteries and their branches.

Seven examples of spasm occurred in six cases of saccular arterial aneurysm of or near the circle of Willis. These were selected from a total group of 29 cases of angiographically demonstrated aneurysms that had recently ruptured. Arteriograms made soon (23 days or earlier) after a subarachnoid hemorrhage from such an aneurysm generally revealed arterial spasm; those made later (26 days or more) revealed none.

Other instances of spasm were associated with total or partial ligation (one each) of the carotid artery in the neck, postoperative astrocytoma, localized intracerebral hemorrhage and edema, and severe intrinsic lesion of the arteries.

The common element in the production of spasm in all cases seemed to be abrupt traction on the arterial wall. Usually the spasm was maximal at the lesion but extended several centimeters along adjacent arteries to a slighter degree. Except in one case, all arteriograms made at the same session revealed the same location and degree of spasm.

ALPERS, Philadelphia.

SUBDURAL HYGROMA COMPLICATING MENINGOCOCCIC MENINGITIS. S. H. STEINBERG and J. P. MURPHY, J. Neurosurg. **8**:671 (Nov.) 1951.

A case of subdural hygroma with membrane formation complicating meningococcic meningitis in a 5-month-old infant is presented.

From a survey of the literature it is apparent that the occurrence of collections of subdural fluid in cases of acute bacterial meningitis is not uncommon, especially in infants 1 year of age or under. The most significant indication of the presence of such fluid is persistent fever after apparent bacteriologic cure. Bulging of the anterior fontanel in an infant also should suggest subdural effusion as a possible cause, if meningitis exists or has existed.

The case here reported represents the early development of a subdural hygroma with rapid recurrence of xanthochromic fluid of high protein content after all cultures had been reported sterile. It was believed that encapsulated fluid was present and that surgical intervention, with removal of the membrane, was necessary.

How subdural hygromas with formation of fluid and organization of membranes complicate successfully treated meningitis is difficult to explain. Complete removal of membranes, with freedom for the growing brain to expand thereafter, is the surgical procedure of choice, if needle aspiration of the subdural fluid cannot keep fluid formation in check.

ALPERS, Philadelphia.

Diseases of the Spinal Cord

PRELIMINARY REPORT ON TREATMENT OF ANTERIOR POLIOMYELITIS WITH EXERCISE AND CURARE. W. D. PAUL and O. A. COUCH JR., Arch. Phys. Med. **30**:277 (May) 1949.

Paul and Couch deduce from animal experimentation that early muscle use is the best means of promoting recovery from peripheral-nerve injury. The patients whom they treated were divided into three groups. In group 1, 21 patients received the routine Kenney treatment, including hot packs and tendon stimulation plus stretching. At the time of admission seven patients of group 2 had varying degrees of stiffness but no paralysis. They were treated by stretching alone, without the use of curare or hot packs. These patients made a rapid and uneventful recovery. In group 3, 26 patients were treated with stretching and use of curare but received no hot packs. Eleven of these had pain and tightness but no paralysis; the other 15 had paralysis. The most important part of the early treatment is the use of exercise or stretching to relieve tightness and pain. When pain makes it impossible to carry out the desired range of motion, administration of curare to the patient makes it possible. Those treated with hot packs and stretching required 9 to 150 days to overcome stiffness and pain. The patients with mild disease, requiring only stretching, were relieved in 2 to 10 days. The group treated by stretching, aided by curare, was relieved of stiffness and pain in 2 to 17 days, except for two patients, who did not have proper stretching. Curare was used only as an aid in carrying out the most important part of the treatment, physical therapy. Excessive doses of the drug may obliterate the resistance felt during stretching, and under these conditions stretching might result in muscle injury.

J. A. M. A.

PARALYTIC POLIOMYELITIS FOLLOWING INJURY. A. BLAIR HARRINGTON, Lancet **1**:987 (May 5) 1951.

Harrington reviewed the records of 100 unselected cases of poliomyelitis acquired during service in the armed forces, in 5 of which there was evidence that trauma had preceded the paralysis. In four of the five cases the disease appeared within 5 days of the injury, in the fifth case, within 11 days. In each case the paralysis appeared in muscles closely related to the site of trauma, the injuries being mostly to the lumbosacral region, with subsequent poliomyelitic involvement of the legs. The author states that apparently trauma upsets the balance between the virus and the host and precipitates the disease.

MADOW, Philadelphia.

SPASTIC PARAPLEGIA IN LATE ADULT LIFE. JOHN D. SPILLANE and GEOFFREY H. T. LLOYD, Lancet **2**:653 (Oct. 13) 1951.

Spillane and Lloyd report 12 cases of spastic paraplegia or tetraplegia due to degeneration and protrusion of cervical intervertebral disks, with resulting compression of the spinal cord. Ten patients were men, and 2, women; the ages ranged from 54 to 70. The duration of symptoms varied from four months to five years. There was a history of injury in one case only. Movements of the neck were usually normal and painless. In all 12 cases there was spastic weakness of the lower limbs, and some abnormalities were noted in the upper limbs in each case, including advanced atrophy with fibrillation of the muscles of the shoulders in five cases.

Lumbar puncture revealed a partial manometric block in only 1 case, with an elevated spinal fluid protein in four cases. In each case there was x-ray evidence of multiple cervical-disk degeneration and prolapse, with arthritic changes in the neurocentral joints and osteophytic projections into the intervertebral foramina and spinal canal. Opaque myelographic studies gave abnormal results in 11 cases. The authors conclude that multiple cervical disk degeneration may lead to bulging of the disks as a whole into the spinal canal. The ridges thus found compress the spinal cord, and abrasive effects on the cord result from friction against this abnormal surface of the spinal canal.

Treatment consisted of bed rest and a neck collar. Two patients had cervical laminectomies, revealing a hard, irregular swelling opposite the disk space between the sixth and the seventh cervical vertebra; but no attempt was made to remove the bony-hard material. Four patients showed definite improvement; four, no change; three were deteriorated, and one died of pneumonia after wearing a collar for eight months, without improvement.

MADOW, Philadelphia.

Peripheral and Cranial Nerves

BILATERAL ULNAR NERVE PALSY AS A RESULT OF PRESSURE PHENOMENON. J. SAEZ and I. D. STEIN, A. M. A. ARCH. INT. MED. **88**:512 (Oct.) 1951.

Isolated peripheral nerve paralysis is common and is most frequently caused by trauma. Multiple peripheral nerve lesions, particularly when symmetrical, are generally ascribed to the effects of a toxin or systemic disease, such as alcoholism, diabetes, or a demyelinating process or virus infection of the central nervous system.

In the case described in this report, ulnar nerve paralysis appeared bilaterally and simultaneously in a sober, industrious 25-year-old man who had recently completed six years of service in the Navy and had returned to college where he spent seven to eight hours a day studying. Symptoms of numbness, tingling, weakness, and atrophy in the distribution of the ulnar nerves appeared about eight months before examination and were progressive in nature.

Roentgenograms of the elbows demonstrated ossicles posterior to the distal end of the humerus on a level with the supratrochlear notch, or foramen. On close questioning, it was learned that at the age of 12 he had injured his right elbow and that the roentgenogram showed "separation or fracture of the right olecranon." Three weeks later he fell and injured the left elbow, and the same roentgenographic appearance of the olecranon was seen on this side. The present abnormal shortening of the olecranon and the identical appearance of the accessory ossicles and their location in respect to the elbow joint probably indicate that the traumas resulted in slipping of the olecranon epiphyses. It is at the age of about 12 years that these epiphyses become united to the shaft.

The ulnar nerve, which is anatomically in a vulnerable position, was left even more unprotected than usual, and the displaced bone fragments were in a position over the ulnar grooves optimal for exerting pressure. The latent period between the time of injury and the appearance of paralysis is probably explained by the recent change in occupation from naval duty to a type of student life which introduced pressure on the elbows for seven to eight hours a day.

Exploration and transposition of the right ulnar nerve were done. The nerve was bound down by fine adhesions. Later, operation was performed on the left ulnar nerve, the nerve being freed and transplanted anteriorly. The postoperative course was uneventful, there being rapid and striking improvement in both motor and sensory functions. After six weeks the left hand was practically normal, the right hand recovering more gradually.

ALPERS, Philadelphia.

PATHOLOGY OF BELL'S PALSY. A. HALL, A. M. A. Arch. Otolaryng. **54**:475 (Nov.) 1951.

Bell's palsy is in all probability a pathogenic entity, the primary and central feature of which is a "dysregulation" of the circulation which probably takes place near the stylomastoid foramen, causing an ischemic paralysis. The consequence of the lack of blood supply to the nerve is edema, with subsequent degenerative changes; the nerve is thus compressed in its bony canal, which causes further impairment of the vascular blood supply, so that a vicious circle arises, the process being reversible.

In a comprehensive paper, Kettel has described 50 consecutive cases in which decompression had been performed. From his observations he concluded that the ischemia near the stylomastoid foramen, which he considered the cause of Bell's palsy, in most cases affects the nerve only as the most susceptible tissue; in other cases, however, the surrounding, more resistant bone is also affected, the result being an ischemic necrosis of bone.

In confirmation of these observations, Hall reports three cases of Bell's palsy in which a resection of the mastoid cells and a decompression of the facial nerve were done. In all cases an exudate was found in the cells at the tip of the mastoid process, and in one case larger cells contained a yellow serous fluid. The bone near the stylomastoid foramen was definitely soft and the facial nerve highly edematous.

ALPERS, Philadelphia.

Muscular System

MYASTHENIA GRAVIS AND MALIGNANT EXOPHTHALMOS. H. ZONDEK and A. TICHO, Lancet **2**:1018 (Dec. 1) 1951.

The authors report the case of a man aged 60 with myasthenia gravis in which malignant exophthalmos gradually developed, despite the usual therapeutic agents. The patient was finally helped by x-irradiation of the pituitary gland. His difficulty began with progressive failure of vision and diplopia; a diagnosis of myasthenia gravis was made, and neostigmine was given by mouth and parenterally. This medication was not very effective and the thymus was irradiated, but this produced only temporary relief. Two years after the onset of his illness he began to lose weight, complained of palpitations, and was found to have an elevated basal metabolic rate. Propylthiouracil was ineffective. Four years after the initial symptoms his eyes began to protrude, and there was progressive lacrimation with conjunctival inflammation. Shortly after this, sugar was found in the urine. He had a myasthenic reaction on electrical stimulation. There was extreme exophthalmos, with loss of all active movement of the eyeballs. The patient could not close the lids completely. There was edema of both legs. Diiodotyrosine and corticotropin were tried without benefit. X-irradiation of the pituitary gland (the roentgenogram of the sella turcica was normal) eventually led to continued improvement in both the myasthenia and the exophthalmos.

The authors believe that the pituitary-diencephalic system was the primary seat of the disturbance, since the patient had the tendency to water edema, diabetes mellitus, and elevated basal metabolic rate.

MADOW, Philadelphia.

Encephalography, Ventriculography and Roentgenography

THE OSSEOUS LESIONS OF TUBEROUS SCLEROSIS. JOHN F. HOLT and WILLARD W. DICKERSON, Radiology **58**:1, 1952.

Holt and Dickerson performed roentgenographic studies on 43 patients for whom an apparently accurate diagnosis of tuberous sclerosis had been made.

The best-known roentgenographic sign of tuberous sclerosis is calcification within the lesions in the brain. This occurred in at least one-half the patients in the authors' group. Three patients had calcification in the dentate nuclei of the cerebellum, and one had calcification in one occipital pole of the brain, identical with that seen in the Sturge-Weber syndrome.

In addition to the intracranial calcifications, 17 of 40 patients with satisfactory roentgenograms of the skull had scattered sclerotic plaques within the cranial vault itself. Postmortem x-ray and pathologic examination of the skull in one case verified the location of the sclerotic plaques within the calvaria.

Twenty of 30 patients whose extremities were examined roentgenographically had definite abnormalities. The changes consisted of cyst-like foci in the phalanges and a rather distinct type of periosteal new-bone formation along the shafts of the metatarsals and the metacarpals. These lesions must be differentiated from those, for example, of sarcoidosis and arthritis, but the authors believe that the changes are sufficiently characteristic to enable the roentgenologist to do this. The cranial plaques or intracranial calcifications which are almost always associated with the lesions in the extremities make the x-ray diagnosis almost certain.

WEILAND, Philadelphia.

Congenital Anomalies

STURGE-WEBER DISEASE AS AN OTOLARYNGOLOGICAL PROBLEM. R. J. MCMAHON, A. M. A. Arch. Otolaryng. **54**:542 (Nov.) 1951.

The pathogenesis of Sturge-Weber disease (nevoid amentia) appears to be a hemangiomatous formation in the layer of mesenchyme directly bordering on the ectoderm, from which are derived the skin in the cephalic region; the mucous membrane of the mouth, nose and throat; the choroid coat of the eye, and the leptomeninges enveloping the brain. Various methods of treatment are described in the literature. The following modalities are most frequently mentioned as therapeutic agents of choice: (1) radiation, including x-rays, radium, and radon; (2) sclerosing solutions (sodium morrhuate); (3) solid carbon dioxide, and (4) direct ligation, excision, or coagulation.

McMahon describes the case of a 9-week-old infant who had had small multiple hemangiomas involving, on the right side, the eyelid, forehead, external ear, scalp, neck, and mucous membranes of the mouth and pharynx since birth. These lesions were increasing in size, and for the past three weeks respiratory distress had been present and was getting progressively worse.

A lateral roentgenogram of the neck suggested a subglottic area of stenosis. Direct laryngoscopy and bronchoscopy demonstrated a subglottic stenosis. Roentgenograms of the skull revealed poorly defined intracranial calcifications in the posterior parietal region on the left side.

Therapy with humidified oxygen and subsequent tracheotomy relieved the respiratory distress. In the light of the intracranial involvement, the prognosis was thought to be poor. The immediate concern was the potency of the airways. It was deemed unwise to remove a biopsy specimen from the subglottic area of stenosis because of the extreme danger of uncontrollable hemorrhage. Needle implantation in this area would be as dangerous as removal of a specimen for biopsy, while application of a radium plaque or of solid carbon dioxide to the stenotic area was mechanically impossible in a patient of this age. With the area of stenosis overlying the vertebral column and being relatively close to the base of the skull, it was thought that cross firing of multiple x-ray parts might endanger nearby growth centers. The patient is to be followed at six-month intervals and subsequent treatments given in the light of survival.

ALPERS, Philadelphia.

LIPID DEGENERATION OF THE NERVOUS SYSTEM: REPORT OF AN ATYPICAL CASE OF AMAUROTIC FAMILIAL IDIOCY. ORLANDO AIDAR and J. LAMARTINE DE ASSIS, Arq. neuro-psiquiat. **9**:276 (Sept.) 1951.

Aidar and de Assis report an atypical case of amaurotic familial idiocy in a 3-year-old white child whose parents were not Jewish. There was no evidence of a cherry-red spot in either retina. The child was admitted with a history of onset of convulsions six months previously. The convulsions came on after an injury to the foot, which was followed by inguinal adenopathy. There was no information as to whether fever was present at the onset of the illness. There was a history of remission for about three months. The patient was unable to walk or stand. Mental changes appeared; the child became dull and apathetic, stopped talking and crying, and swallowed with difficulty. Examination showed a dull child who was indifferent, did not talk or cry, and overreacted to external stimuli. It was difficult to determine whether she was blind. There was spastic paresis of all four limbs, a bilateral Babinski sign, generalized hyperreflexia, and cutaneous hyperesthesia. The Kahn and Wassermann reactions of the blood were negative. There was mild secondary anemia and lymphocytosis. The spinal fluid showed 53

lymphocytes per cubic millimeter; the total protein was 20 mg., the sugar 77 mg. and the chlorides 690 mm., per 100 cc. The Rh factor was negative. The fundi showed no changes. The child died of pneumonia eight months after onset of illness, which was characterized by remissions and exacerbations. During exacerbations there was usually a rise in temperature. Typical changes of amaurotic familial idiocy were found in the nervous system.

N. Savitsky, New York.

Diseases of the Skull and Vertebrae

Neurologic Complications Associated with Hereditary Deforming Chondrodysplasia. A. Slepian and W. B. Hamby, J. Neurosurg. **8**:529 (Sept.) 1951.

Hereditary deforming chondrodysplasia is described as a congenital abnormality of osteochondral development, causing irregularity and arrest in growth at the metaphyseal ends of long bones, with resulting deformity and the occurrence of multiple cartilaginous masses, which, with calcification, become osteocartilaginous.

Neurologic complications of this disease are rare. Approximately 1,000 cases of hereditary deforming chondrodysplasia have been reported, in only 19 of which neurologic complications were found. The authors report 2 new cases of such complications in brothers, making a total of 21.

In their first patient an exostosis of the cervical vertebrae compressed the spinal cord; in the second an exostosis of the femur compressed the sciatic nerve. Two children of the second patient also bear uncomplicated stigmata of the disease.

In the literature males were involved in 14 of 15 reported cases in which the sex was mentioned. The spinal cord was involved in 10 cases; the sciatic nerve, in 6; the peroneal nerve, in 2, and the brachial plexus and ulnar nerve, in 1 case each. Alpers, Philadelphia.

Ocular and Trigeminal Involvement as the Presenting Syndrome of Myeloma of the Petrous Bone. Delmas-Marsalet, Pauly, Leger, Pouyanne, and Leman, Rev. oto-neuro-oftal. **32**:411 (Oct.) 1951.

An unusual case is reported in which the first symptoms of multiple myeloma were involvement of the third and fifth cranial nerves on one side.

A man aged 64 became ill with diplopia, which lasted a month; supraorbital pain appeared on the left side at the same time. Ptosis was noted six months later. Examination at this time showed paralysis of the left third and sixth cranial nerves, intact pupils, and diminution of the left corneal reflex without sensory changes in the face. Exudates were noted in both fundi, with diminished visual acuity and a blood pressure of 160/60. The Wassermann reactions of the spinal fluid and the blood were negative, with 0.66 cell per cubic millimeter of spinal fluid. X-ray studies showed destruction of the left petrous tip and decalcification of the sella and sphenoid sinus. Extradural exploration of the middle fossa on the left side showed nothing abnormal. X-ray treatments were given to the middle fossa, to which the patient responded. Three weeks later he felt much better; the ptosis disappeared, and there was no longer any ocular pain. There was recurrence of headache and right ptosis in three months. The patient was readmitted to the hospital, at which time examination showed ptosis of the right eyelid and paralysis of the right superior rectus; the right pupil was wider than the left, but both reacted well to light and in accommodation; there was bilateral corneal hypalgesia. The globulin in the blood was increased, and the reaction to the Bence Jones test was negative. A defect was found in the left frontal region of the skull. Defects in the bones were also found in the lumbar portion of the spine, in the pelvis, and in both tibiae. Biopsy of the frontal bone at the site of the defect showed myeloma. This diagnosis was confirmed by bone-marrow puncture.

N. Savitsky, New York.

Books

Clinical Sonnets. By Merrill Moore, M.D. Third Printing. Price, $2.50. Pp. 72. Wayne Publishers, Inc., 42 Broadway, New York 4, 1950.

Merrill Moore has written thousands of sonnets and published five books of them. The form is not orthodox, and the author agrees that they are illegitimate; but one can leave that argument to the professors of literature. This little book, of sixty-one sonnets, is written as a doctor, depicting the people he has seen. In his own words, "I have begun to use the sonnet as a portrait lens to portray personality." This he has done most successfully, with humor and poignancy. To the physician they make diverting reading, because the terse, rhythmic descriptions bring back to memory, with a jolt, patients that have passed his doors.

Shock Treatments, Psychosurgery and Other Somatic Treatments in Psychiatry. Second Edition. By Lothar B. Kalinowsky, M.D., and Paul H. Hoch, M.D. Price, $8.75. Pp. 396. Grune & Stratton, Inc., 381 4th Ave., New York 16, 1952.

Developments in the field of shock therapy and psychosurgery have been so extensive in the six years since the publication of the first edition of this work that the present volume has doubled in size. As the authors say in their preface, "The title was changed to include psychosurgery, which, together with the shock treatments has assumed a prominent place among the somatic treatments in psychiatry. . . . The subject is now being presented in the same manner in which shock treatments are discussed, combining an objective survey of the literature with an account of the authors' own experience and their personal views on many of the controversial issues."

The personal views are presented with unusual clarity and show evidence not only of considerable thought, but of actual experience. The chapters on insulin shock therapy and convulsive shock therapy are practical and eminently readable. Combined insulin-electric shock therapy is revealed as still in the stage of development, with no systematization yet possible. Indications and contraindications are systematically presented, together with suggestions for overcoming some of the difficulties in the various stages of treatment and a frank recognition of the impossibility of curing everybody. The emphasis is upon early and adequate treatment. Psychotherapy is accorded a definite role in connection with the treatments, although the authors caution against excessive optimism until after the shock treatments have presented the psychotherapist with a patient in satisfactory condition for association and transference. The authors are oriented along somatic lines, and the reader gets the impression that psychotherapy is all right so far as it goes but may be used indiscriminately in unsatisfactory cases, just as shock therapy is.

Psychosurgery is reviewed in competent fashion. The authors point out that restricted operations are valuable in patients without great disorganization of the personality, whereas a major lobotomy is the only answer to the problem presented by some of the severely disturbed schizophrenic patients. They are rather partial to the transorbital method, with its greater safety and freedom from complications.

Carbon dioxide therapy is given small place among the other somatic treatments, which also include pharmacotherapy, fever therapy, sleep, use of hormones, refrigeration, photoshock, and a dozen other modifications. In spite of extensive activity in the field of somatic treatments, it is impossible for two men to try everything. The personal experience is what counts. The chapter on theoretical considerations leaves the reader bewildered. "The discussion of the theoretical aspects of various somatic treatments has shown that most of them are poorly understood, or, as in the case of shock treatments, still entirely obscure in their mode of action." The authors mention the fifty theories collected by Gordon. There is a bibliography of more than fifty pages.

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